SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Acculink

Device Trade Name: RX Acculink® Carotid Stent System (RX Acculink)

Applicant's Name and Address: Abbott Vascular
3200 Lakeside Drive
Santa Clara, CA 95054

Date of Panel Recommendation: January 26, 2011

Premarket Approval Application (PMA) Number: P040012/S034

Date of FDA Notice of Approval: May 6, 2011

Expedited: Not applicable

The original PMA (P040012) was approved on August 30, 2004 and is indicated as follows:

> The RX Acculink Carotid Stent System, used in conjunction with Abbott Vascular's Accunet or Emboshield family of Embolic Protection Systems (EPS), is indicated for the treatment of patients at high risk for adverse events from carotid endarterectomy who require carotid revascularization and meet the criteria outlined below:
>
> 1. Patients with neurological symptoms and ≥ 50% stenosis of the common or internal carotid artery by ultrasound or angiogram OR patients without neurological symptoms and ≥ 80% stenosis of the common or internal carotid artery by ultrasound or angiogram, AND
> 2. Patients must have a reference vessel diameter within the range of 4.0 mm and 9.0 mm at the target lesion.

The SSED to support the indication is available on the CDRH website and is incorporated by reference here. The current supplement was submitted to expand the indication for the RX Acculink Carotid Stent System to include patients at standard risk for adverse events from carotid endarterectomy.

II. INDICATIONS FOR USE

The RX Acculink Carotid Stent System, used in conjunction with the Abbott Vascular embolic protection system specified below, is indicated for the treatment of patients at

high and standard risk for adverse events from carotid endarterectomy who require carotid revascularization and meet the criteria outlined below:

	High Risk	Standard Risk
Embolic Protection System	Abbott Vascular's Accunet or Emboshield Family	Abbott Vascular's Accunet only
With neurological symptoms	≥ 50% stenosis of the common or internal carotid artery by ultrasound or angiogram	≥ 70% stenosis of the common or internal carotid artery by ultrasound or ≥ 50% stenosis of the common or internal carotid artery by angiogram
Without neurological symptoms	≥ 80% stenosis of the common or internal carotid artery by ultrasound or angiogram	≥ 70% stenosis of the common or internal carotid artery by ultrasound or ≥ 60% stenosis of the common or internal carotid artery by angiogram
Reference vessel diameter	Must be within 4.0 mm – 9.0 mm at the target lesion	

III. CONTRAINDICATIONS

The RX Acculink Carotid Stent System is contraindicated for use in:

- Patients in whom anti-coagulant and / or anti-platelet therapy is contraindicated.
- Patients with severe vascular tortuosity or anatomy that would preclude the safe introduction of a guide catheter, sheath, embolic protection system, or stent system.
- Patients with known hypersensitivity to nickel-titanium.
- Patients with uncorrected bleeding disorders.
- Lesions in the ostium of the common carotid artery.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the RX Acculink Carotid Stent System labeling.

V. DEVICE DESCRIPTION

The RX Acculink Carotid Stent Systems are designed to deliver nitinol self-expanding stents, designed to maintain patency of obstructed carotid arteries, via a sheathed delivery system. The stent systems are equivalent in design to the RX Acculink Stent Systems market approved for the high surgical risk population.

The RX Acculink Carotid Stent System is comprised of two main components:

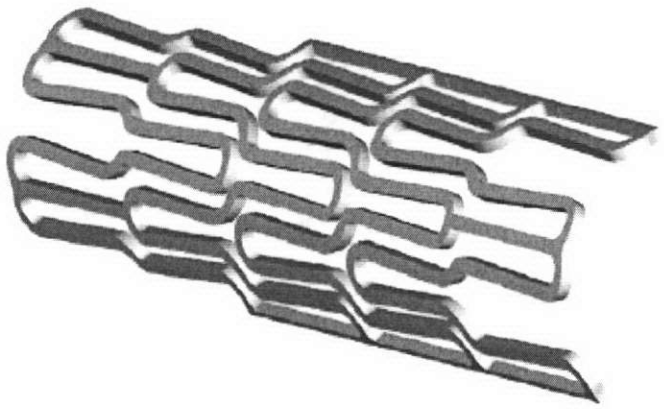
- the stent (Acculink Carotid Stent)
- the delivery system (RX Acculink Stent Delivery System)

A. Acculink Carotid Stent

The Acculink Carotid Stent is a nickel-titanium, self-expanding stent. The Acculink Carotid Stent is available in diameters of 5, 6, 7, 8, 9, and 10 mm and lengths of 20, 30, and 40 mm in a straight configuration; a tapered configuration is available in diameters from 6-8 mm and 7-10 mm, each available in lengths of 30 and 40 mm.

The stent is implanted into a target vessel, which is smaller than the stent diameter, so that the stent applies a force to the vessel to keep it open.

Figure 1: RX Acculink Carotid Stent Geometric Model (20mm Stent Length)



The device is available in the following sizes:

Table 1: RX Acculink Carotid Stent System – Stent Diameters

Unconstrained Stent Diameter (mm)	Stent Length (mm)	Reference Vessel Diameter (mm)
5.0	20, 30, 40	3.6 – 4.5
6.0	20, 30, 40	4.3 – 5.4
7.0	20, 30, 40	5.0 – 6.4
8.0	20, 30, 40	5.7 – 7.3
9.0	20, 30, 40	6.4 – 8.2
10.0	20, 30, 40	7.1 – 9.1

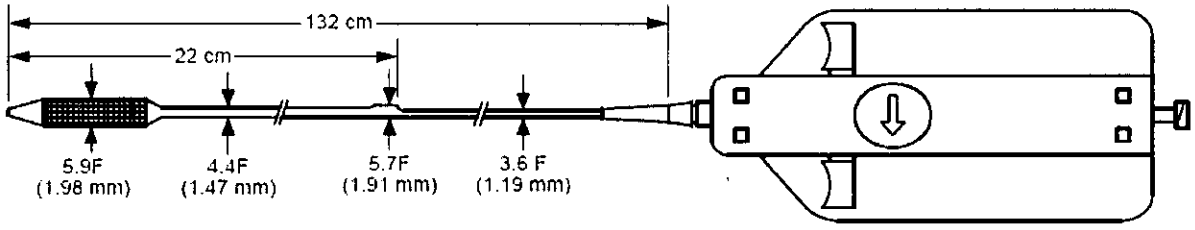
Table 2: RX Acculink Carotid Stent System – Tapered Stent Diameters

Unconstrained Stent Diameter (mm)	Stent Length (mm)	ICA Reference Vessel Diameter (mm)	CCA Reference Vessel Diameter (mm)
6 – 8 Taper	30, 40	4.3 – 5.4	5.7 – 7.3
7 – 10 Taper	30, 40	5.0 – 6.4	7.1 – 9.1

B. RX Acculink Stent Delivery System

The Rapid Exchange (RX) Acculink Stent Delivery System, is a single-use device that uses a sheath to mechanically constrain the Acculink Carotid Stent at a small diameter for delivery to the treatment site. The system is inserted through a guide catheter or sheath, and is tracked over a 0.014" guide wire. Radiopaque markers located on the delivery system at the proximal and distal ends of the stent, aid in accurate placement of the stent in the lesion.

Figure 2: RX Acculink Carotid Stent System – Delivery System Schematic



VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of carotid artery disease:

- Surgery (endarterectomy)
- Medical therapy (use of antiplatelet and/or anticoagulant medicine, as well as antihypertensive and antilipidemic drugs as indicated)
- A combination of surgery and medical therapy
- Modification of lifestyle risk factors for stroke, such as cigarette smoking and alcohol use, can lower the risk of stroke

Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The RX Acculink Carotid Stent System is commercially available in the European Economic Area (EEA), Australia, and other countries. On August 30, 2004, the RX Acculink Carotid Stent System was approved for marketing in the United States for use in the high surgical risk population. The stent systems approved for the standard surgical risk population under this PMA Supplement are identical to those market approved for the high surgical risk population.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device:

- Allergic reactions to anti-platelet agents / contrast medium
- Aneurysm
- Angina / coronary ischemia
- Arrhythmia
- Arterial occlusion / thrombosis at puncture site or remote site
- Arteriovenous fistula
- Bacteremia or septicemia
- Bleeding from anticoagulant or antiplatelet medications
- Cerebral edema
- Cerebral hemorrhage
- Cerebral ischemia / transient ischemic attack (TIA)
- Congestive heart failure (CHF)
- Death
- Detachment and / or implantation of a component of the system
- Emboli, distal (air, tissue or thrombotic emboli)
- Emergent or urgent endarterectomy surgery (CEA)
- Fever
- Filter thrombosis / occlusion
- Groin hematoma, with or without surgical repair
- Hemorrhage, with or without transfusion
- Hyperperfusion syndrome
- Hypotension / hypertension
- Infection and pain at insertion site
- Ischemia / infarction of tissue / organ
- Myocardial infarction (MI)
- Pain (head, neck)
- Pseudoaneurysm, femoral
- Renal failure / insufficiency
- Restenosis of stented segment
- Seizure
- Severe unilateral headache
- Stent / filter entanglement / damage
- Stent embolization
- Stent malposition
- Stent migration
- Stent thrombosis / occlusion
- Stroke / cerebrovascular accident (CVA)
- Total occlusion of carotid artery
- Vessel dissection, perforation, or rupture
- Vessel spasm or recoil

For the specific adverse events that occurred in the clinical studies, please see Section X below.

IX. SUMMARY OF PRECLINICAL STUDIES

No new preclinical studies were submitted or required for the approval of the expanded indication proposed in this PMA supplement. Please see the original SSED for details of the non-clinical testing that was conducted to obtain approval of P040012.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study in the US and Canada under IDE # G000080 to establish a reasonable assurance of safety and effectiveness of carotid stenting using the Acculink Carotid Stent System for the treatment of patients at standard risk for adverse events from carotid endarterectomy who require carotid revascularization and meet the criteria specified in the indication. The Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST) was a prospective, randomized, two-arm multi-center trial, with blinded endpoint evaluation. Data from this clinical study were the basis for the PMA Supplement approval decision. A summary of the clinical study is presented below.

A. Study Design

Enrollment in CREST began on December 21, 2000 and the last patient was enrolled on July 18, 2008. The database for this PMA supplement reflected data collected through March 26, 2010 and included 2502 patients. There were 116 investigational sites in the United States and Canada.

Subjects were treated prospectively with either carotid endarterectomy (CEA), the current standard of care for subjects with stenosis of the internal carotid artery at standard risk of adverse events, which served as the control arm in the study, or with carotid artery stenting (CAS) using the Abbott Vascular devices. The commercially available Acculink and RX Acculink Carotid Stent Systems and Accunet and RX Accunet Embolic Protection Devices (EPDs) were used during the trial. P040012/S034 seeks approval for an expanded indication for the RX Acculink Carotid Stent System based on the CREST data. The Acculink and RX Acculink differ only with respect to their delivery systems. The Acculink system uses an over-the-wire delivery system, and the RX Acculink uses a rapid exchange delivery system. Since the devices are otherwise similar, FDA did not have concerns with using the combined Acculink and RX Acculink data to support approval of the expanded RX Acculink indication. The primary endpoint events, including death, stroke, and myocardial infarction within 30 days and ipsilateral stroke occurring between 31 and 365 days of the study procedure have historically been used to assess the safety and effectiveness of carotid stenting in symptomatic and asymptomatic patient populations.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the CREST study was limited to patients who met the inclusion criteria outlined in the table below. Patients were not permitted to enroll in the CREST study if they met any of the exclusion criteria outlined in the table below.

Table 3: CREST Inclusion and Exclusion Criteria

Category	Symptomatic	Asymptomatic
Age	• Subjects > 18 years old	
Symptomatic Status	• Subject with history of TIA, amaurosis fugax, minor or non-disabling stroke within 180 days of randomization date • Subjects were excluded with: o Evolving stroke o Stroke within 7 days putting subject at risk for hemorrhagic conversion o Ischemic stroke with hemorrhagic transformation within 60 days	• Not symptomatic
Carotid Stenosis	• Stenosis ≥ 50% defined as: o Stenosis ≥ 50% by angiography **or** o Stenosis ≥ 70% by ultrasound **or** o Stenosis ≥ 70% by MRA or CTA confirmed by radiologist (if 50-69% by ultrasound)	• Stenosis > 60% defined as: o Stenosis ≥ 60% by angiography **or** o Stenosis ≥ 70% by ultrasound **or** o Stenosis ≥ 80% by MRA or CTA confirmed by radiologist (if 50-69% by ultrasound)
Vessel Characteristics	• Discrete lesion in ICA with or without involvement in CCA • Vessel diameter > 4.0 mm and < 9.0 mm from reference or contralateral artery • Absence of excessive vessel tortuosity that would impede delivery of devices	
Medical Condition	Symptomatic and asymptomatic subjects were excluded with 1 or more of the following: • Knowledge of two or more proximal or major diseased coronary arteries with ≥ 70% stenosis that have not, or cannot be revascularized • Ejection fraction < 30% or New York Heart Association (NYHA) Functional Class III or higher • Unstable angina defined as rest angina with ECG changes • Currently listed for major organ transplantation or being evaluated for such • Malignancy or respiratory insufficiency limiting life expectancy to < 5 years or FEV1< 30% (predicted) • Dialysis dependent renal failure • Uncontrolled diabetes defined as fasting glucose > 400 mg/dl and ketones > +2 • Concurrent requirement for any surgery requiring general anesthesia	
CEA (Additional eligibility for CEA arm only)	• Subject was a candidate for CEA and met all other eligibility criteria • CEA were excluded with: o Status/post radiation treatment to the neck o Status/post radical neck surgery o Surgically inaccessible lesion (i.e. lesions above C2) o Spinal immobility – inability to flex neck beyond neutral or kyphotic deformity o Symptomatic, well-delineated carotid artery dissection below carotid siphon o Ostial lesion of LCCA/RCCA below clavicle o Presence of tracheostomy stoma o Contralateral laryngeal nerve paralysis o Previous CEA, extracranial-intracranial or subclavian bypass ipsilateral to carotid stenosis	
Neurologic	• Ability to understand and cooperate with study procedure • Symptomatic and asymptomatic subjects were excluded with: o Severe dementia o Neurologic illnesses within past 2 years which could not be distinguished from a TIA or stroke o History of major ipsilateral stroke likely to confound study endpoints • History of spontaneous intracranial hemorrhage within past 12 months	
Cardiac	Symptomatic and asymptomatic subjects were excluded with: • Myocardial infarction within previous 30 days • Knowledge of cardiac sources of emboli • Chronic atrial fibrillation • Any episode of paroxysmal atrial fibrillation within past 6 months or history of such requiring chronic anticoagulation	
Blood Abnormality	Symptomatic and asymptomatic subjects were excluded with: • Hgb < 10 g/dL, platelet count < 125,000/μL, uncorrected INR > 1.5, bleeding time >1 minute beyond upper limit normal, or heparin-associated thrombocytopenia • Active bleeding diathesis or coagulopathy or subject would refuse blood transfusions	
Medications	Symptomatic and asymptomatic subjects were excluded with: • Recent GI bleed that would interfere with antiplatelet therapy	

Category	Symptomatic	Asymptomatic
	• Known untoward reaction to anesthesia not able to be overcome by pretreatment with medications • History of intolerance or allergic reaction to any study medication including ASA, ticlopidine and clopidogrel	
Angiography	Symptomatic and asymptomatic subjects who had angiography prior to randomization were excluded with: • Severe vascular tortuosity or anatomy precluding safe introduction of guiding catheter / sheath or stent placement • Presence of a previously placed intravascular stent or graft in the ipsilateral artery • Presence of extensive or diffuse atherosclerotic disease involving the aortic arch and proximal common carotid artery precluding safe introduction of guiding catheter / sheath • An intraluminal filling defect that was not associated with an ulcerated target lesion • Abnormal angiographic findings constituting a contraindication to CEA • Bilateral carotid stenosis if intervention was planned within the 30-day CREST peri-procedural period • Occlusion "string sign" >1 cm of the ipsilateral common or internal carotid artery	

2. Follow-up Schedule

A 24-hour post-procedural neurological assessment was required prior to hospital discharge in order to assure detection of early post-procedural strokes.

All patients were scheduled to return for follow-up examinations at 30 days, 6 months, 12 months, 18 months and annually until study exit. Telephone contact was scheduled at 2 weeks, 3 months, and 9 months, and annually thereafter.

The following table provides a summary of the required clinical and laboratory tests for both CAS and CEA subjects:

Table 4: CREST Clinical and Laboratory Tests

Test	Pre-Procedure	Post-Procedure	Post-Discharge
Carotid duplex ultrasound	√[1]		1, 6, 12 months, yearly thereafter
CT scan/MRI	√[1]		PRN[1]
Neurological exam	√[2]	√[2]	1 and 12 months[2]
NIH Stroke Scale (NIHSS)	√[2]	√[2]	1, 6 and 12 months[2,5]
Modified Rankin Scale	√		1, 6 and 12 months
Barthel Index	√		1, 6 and 12 months
Quality of Life Scales	√		2 weeks, 1 month and 1 year
Medical History, Risk Factor Profile	√		1, 3, 6, 9, 12 months and yearly thereafter
ECG	√	√[3]	1 month[3]
Cardiac Biomarkers (CPK, CK-MB or troponin)	√	√[4]	None
Lipid Profile	√		6, 12 months and yearly thereafter
SMAC-7	√		6, 12 months and yearly thereafter
Fasting Blood Sugar	√		6, 12 months and yearly thereafter
Cerebral Angiogram	√[1]		PRN

[1] Most recent pre-procedural neurological image was used for baseline (if available), and additional CT scans were performed as needed to evaluate subsequent cerebrovascular events.

[2] Neurological examinations performed pre-procedure, immediately post-procedure, and at 1 and 12 month follow-up visits were performed by the independent study neurologist or neurosurgeon certified in the use of the NIHSS. This physician was not the physician who performed the study procedure.

[3] In addition to post-procedure ECG, an ECG was obtained for chest pain lasting more than 15 minutes or for symptoms indicating myocardial ischemia.

[4] In addition to post-procedure cardiac biomarkers (CPK, CK-MB, or troponin), cardiac biomarkers were repeated every 8 hours x 3 with pathological elevation of post-procedure biomarkers, for ECG changes or for chest pain lasting more than 15 minutes.

[5] A NIHSS was assessed 3 months after the occurrence of a potential stroke occurring with 12 months of the study procedure. At the 6 month follow-up visit, the NIHSS could be administered by a health care professional on the study staff who was certified in the use of the NIHSS if the independent study neurologist/neurosurgeon was not available.

Adverse events and complications were recorded at all visits.

The key endpoints are shown below in the tables summarizing safety and effectiveness.

3. Clinical Endpoints

The primary safety and effectiveness endpoint of CREST was the composite of death, stroke and myocardial infarction (DSMI) at 30 days plus stroke ipsilateral to the study artery between 31 and 365 days. Key additional analyses included the 1-year composite endpoint by strata defined by symptomatic status and octogenarian status, peri-procedural DSMI at 30 days, target lesion revascularization (TLR) at 12 months, access site complications, cranial nerve injury and the composite endpoint of DSMI at 30 days plus stroke ipsilateral to study artery after 31 days.

The study protocol design defined study success as CAS being non-inferior to CEA when measured by the primary endpoint.

- Pre-Specified Statistical Analysis Plan
  The null hypothesis was that the CAS arm was worse than the CEA arm by a pre-specified non-inferiority margin of 2.6% (i.e., the event rate for the CAS arm was greater than or equal to the event rate for the CEA arm plus a non-inferiority margin of 2.6%). The null hypothesis was rejected based on a non-inferiority analysis.

  The primary endpoint analysis was performed based on the Per-Protocol (PP) analysis population. The Intent-to-Treat (ITT) population was also evaluated. In addition, a propensity score-adjusted non-inferiority analysis was performed on the PP population. The propensity score was estimated from logistic regression using baseline characteristics and medical history data for age, gender, symptomatic status, prior CAD, CABG, diabetes, dyslipidemia, hypertension, smoking, and pre-procedure target lesion percentage diameter stenosis.

  Non-inferiority tests were also performed for the:
  - 1 year composite endpoint by strata defined by symptomatic status
  - Peri-procedural endpoint events
  - 4 year composite endpoint rate
  - 1 year composite endpoint for non-octogenarian subjects

- External Evaluation Groups
  All primary endpoint events (death, MI, and all potential strokes) were adjudicated by a Clinical Events Committee (CEC). The angiograms, carotid duplex ultrasounds, and electrocardiograms were assessed by central core laboratories. An NIH-appointed Data Safety Monitoring Board assessed the ongoing safety of CREST.

- Study Design Discussion
  CREST compared the safety and effectiveness of carotid artery stenting (CAS) to carotid endarterectomy (CEA) in symptomatic and asymptomatic subjects deemed to be eligible for CEA and at standard risk for complications from surgery at 1 year (death, stroke and MI at 30 days plus ipsilateral stroke between 31 and 365 days). Eligible subjects were randomly assigned in a 1:1 ratio to CAS or CEA, with stratification according to the clinical center and subject's symptomatic status. Recruitment restrictions were imposed to ensure that the proportion of symptomatic subjects was between 800 (32%) and 1700 (68%) of the total study population at the conclusion of the study. CREST evaluated strokes between 31 and 365 days as an effectiveness measure. Death, stroke and MI at 30 days were the primary safety measure.

All potential primary endpoint events were independently adjudicated by a CEC.

CREST evaluated potential MI based on the assessment of prospectively collected ECG, cardiac biomarker data in addition to clinical symptoms.

B. Accountability of PMA Cohort

At the time of database lock, of the 2502 randomized subjects enrolled in the PMA study at 107 clinical sites in the United States and 9 sites in Canada, 96.0% (2365/2464) of subjects at 1 month and 90.3% (2140/2369) of subjects at 1 year post-procedure were available for analysis.

Long-term follow-up is available for 82.3% (1770/2150) of subjects at 2 years, 78.9% (1179/1494) of subjects at 3 years, and 72.4% (589/813) of subjects at 4 years. The follow-up rates are balanced between the CAS and CEA arms at all scheduled follow-up intervals as indicated below in Table 5.

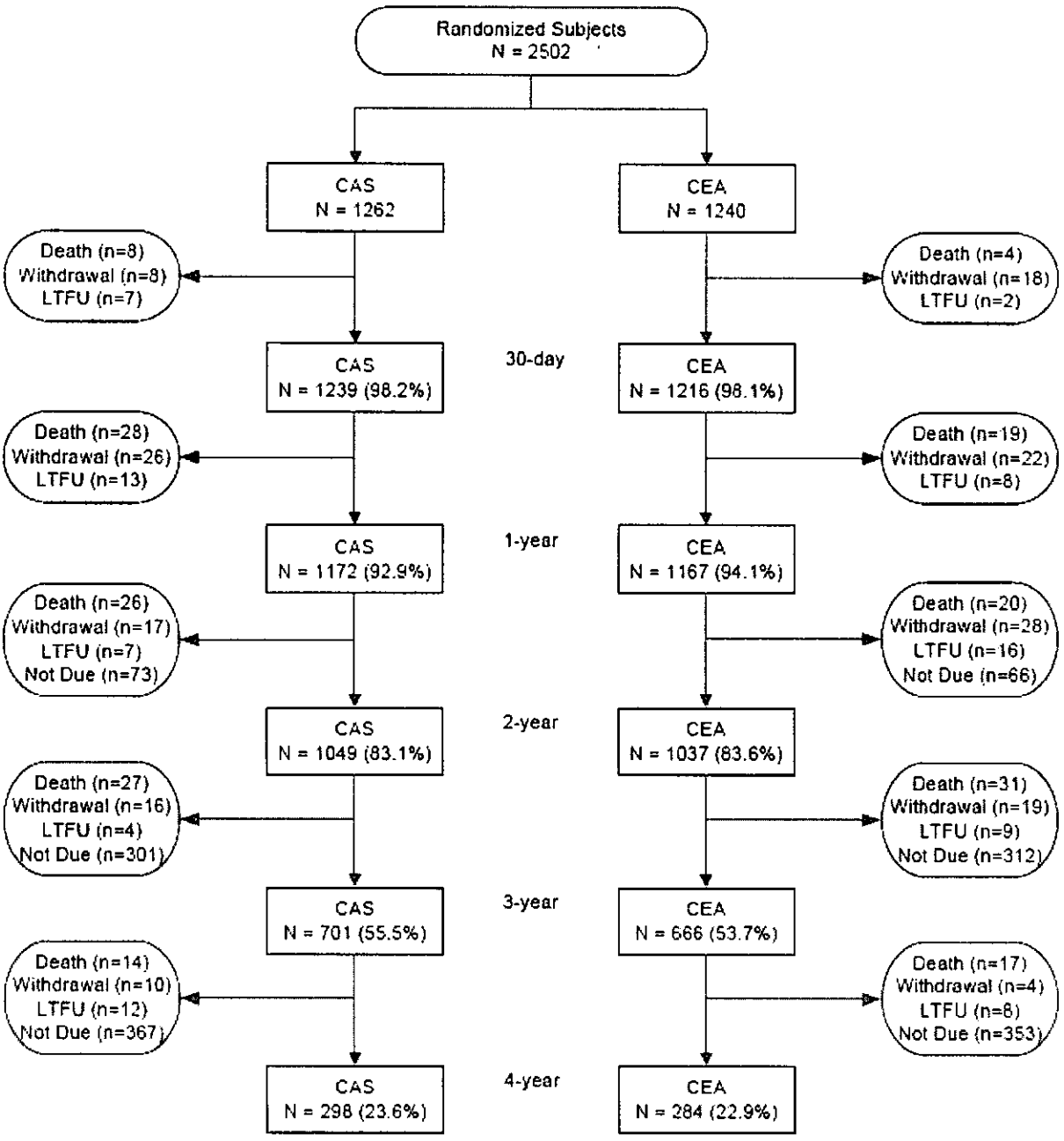
Table 5: Summary of Follow-Up Assessment for All Randomized Subjects

		CAS N=1262	CEA N=1240	Total N=2502
30 Days	Subjects Followed-up	1195	1170	2365
	Percent (Followed-up/Eligible[1])	95.9%	96.1%	96.0%
12 Months	Subjects Followed-up	1080	1060	2140
	Percent (Followed-up/Eligible)	90.6%	90.1%	90.3%
48 Months	Subjects Followed-up	306	283	589
	Percent (Followed-up/Eligible)	73.4%	71.5%	72.4%

[1]Patients who died or withdrew their consent prior to the visit or who had not yet reached that follow-up time point were not considered eligible. Please see Figure 3 below.

Figure 3 shows subject accountability for the CAS and CEA arms at various important study intervals. Figure 3 includes subjects censored only up to 4 years, and therefore does not include subjects contributing data during the 48-month (+ 6 week) follow-up window or thereafter (who are included in Table 5).

Figure 3: Subject Accountability in the CAS and CEA Arms (N=2502)



Notes:

- The denominators for determination of number of subjects participating at each time point are CAS = 1262 and CEA = 1240.
- The number of subjects who expired, withdrew, were lost to follow-up or not due for follow-up are reflective of each time interval (not cumulative).

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a carotid artery stenting study performed in the US.

Key baseline demographics and risk factors were comparable between CAS and CEA and are shown in Table 6 for all CREST randomized subjects. The calculated difference with 95% confidence intervals between the two study arms suggests that data for CREST subjects randomized to CAS and CEA were balanced in all the key demographic categories.

The mean age was 69.1 years and 9.7% (243/2502) of the study population were octogenarians. Male subjects comprised 65.1% (1630/2502) of the study population which is consistent with recently published data from an observational study in which 60.9% of subjects with atherosclerotic lesions who underwent CAS were male [J Vasc Surg 51(5): 1116-1123 (2010)]. This is also consistent with the 66%-78% proportion of males enrolled in several randomized CAS and CEA clinical trials that studied similar patient populations.

Baseline characteristics that occurred most frequently in greater than 10% of the CREST population were prior cardiovascular disease 43.7% (1046/2394), previous CABG 20.7% (514/2480), diabetes using oral anti-diabetic agents only 22.8% (567/2488), hypertension 85.9% (2141/2492), dyslipidemia 84.4% (2093/2481) and history of / or current smoker 65.7% (1619/2465).

Table 6: Baseline Demographics and Medical History for All Randomized Subjects (N = 2502)

	CAS N = 1262	CEA N = 1240	Total N = 2502	Difference [95% CI]
Mean Age ± SD (N) Median Range (min, max) [95% Conf. Interval]	68.9 ± 9.0 (1262) 69.1 (39.8, 96.2) [68.4, 69.4]	69.2 ± 8.8 (1240) 70.0 (40.7, 91.5) [68.7, 69.7]	69.1 ± 8.9 (2502) 69.7 (39.8, 96.2) [68.7, 69.4]	-0.3 [-1.0, 0.4]
Age ≥ 80 years [95% Conf. Interval]	10.2% (129/1262) [8.6%, 12.0%]	9.2% (114/1240) [7.6%, 10.9%]	9.7% (243/2502) [8.6%, 10.9%]	1.0% [-1.3%, 3.3%]
Male [95% Conf. Interval]	63.9% (807/1262) [61.2%, 66.6%]	66.4% (823/1240) [63.7%, 69.0%]	65.1% (1630/2502) [63.2%, 67.0%]	-2.4% [-6.2%, 1.3%]
Symptomatic [95% Conf. Interval]	52.9% (668/1262) [50.1%, 55.7%]	52.7% (653/1240) [49.8%, 55.5%]	52.8% (1321/2502) [50.8%, 54.8%]	0.3% [-3.6%, 4.2%]
Prior Cardiovascular Disease [95% Conf. Interval]	42.4% (514/1211) [39.6%, 45.3%]	45.0% (532/1183) [42.1%, 47.9%]	43.7% (1046/2394) [41.7%, 45.7%]	-2.5% [-6.5%, 1.4%]
Aortic / Mitral Valvular Disease [95% Conf. Interval]	5.8% (72/1231) [4.6%, 7.3%]	4.4% (54/1215) [3.4%, 5.8%]	5.2% (126/2446) [4.3%, 6.1%]	1.4% [-0.3%, 3.2%]
Previous CABG [95% Conf. Interval]	19.9% (249/1250) [17.7%, 22.2%]	21.5% (265/1230) [19.3%, 23.9%]	20.7% (514/2480) [19.1%, 22.4%]	-1.6% [-4.8%, 1.6%]
Cardiac Arrhythmia [95% Conf. Interval]	6.0% (75/1240) [4.8%, 7.5%]	6.5% (79/1210) [5.2%, 8.1%]	6.3% (154/2450) [5.4%, 7.3%]	-0.5% [-2.4%, 1.4%]
Presence of Left Ventricular Hypertrophy [95% Conf. Interval]	6.1% (69/1127) [4.8%, 7.7%]	5.7% (63/1104) [4.4%, 7.2%]	5.9% (132/2231) [5.0%, 7.0%]	0.4% [-1.5%, 2.4%]
Diabetes Mellitus [95% Conf. Interval]	30.5% (384/1257) [28.0%, 33.2%]	30.4% (375/1232) [27.9%, 33.1%]	30.5% (759/2489) [28.7%, 32.3%]	0.1% [-3.5%, 3.7%]
Hypertension [95% Conf. Interval]	85.8% (1080/1259) [83.7%, 87.7%]	86.1% (1061/1233) [84.0%, 87.9%]	85.9% (2141/2492) [84.5%, 87.3%]	-0.3% [-3.0%, 2.5%]
Dyslipidemia [95% Conf. Interval]	82.9% (1040/1254) [80.7%, 85.0%]	85.8% (1053/1227) [83.7%, 87.7%]	84.4% (2093/2481) [82.9%, 85.8%]	-2.9% [-5.7%, -0.0%]
History of / or Current Cigarette/Cigar Smoking [95% Conf. Interval]	65.2% (811/1244) [62.5%, 67.8%]	66.2% (808/1221) [63.4%, 68.8%]	65.7% (1619/2465) [63.8%, 67.6%]	-1.0% [-4.7%, 2.8%]
Family History of Stroke [95% Conf. Interval]	32.2% (339/1052) [29.4%, 35.1%]	32.7% (339/1037) [29.8%, 35.6%]	32.5% (678/2089) [30.4%, 34.5%]	-0.5% [-4.5%, 3.5%]
Prior Contralateral CEA [95% Conf. Interval]	4.5% (57/1257) [3.5%, 5.8%]	5.2% (64/1230) [4.0%, 6.6%]	4.9% (121/2487) [4.1%, 5.8%]	-0.7% [-2.4%, 1.0%]

Symptomatic and Asymptomatic Subjects

Of the randomized study subjects enrolled in the trial, 52.8% (1321/2502) were symptomatic subjects and 47.2% (1181/2502) were asymptomatic subjects, as shown in Table 7. The enrollment was well balanced between the symptomatic and asymptomatic subgroups. The recruitment restriction for enrollment of between 800 (32.0%) and 1700 (68.0%) symptomatic subjects was satisfied. Within each of the symptomatic and the asymptomatic subgroups, subjects were evenly randomized between the CAS and the CEA treatment arms.

Table 7: Subject Enrollment by Symptomatic Status

Analysis Population	Symptomatic Subjects			Asymptomatic Subjects		
	CAS	CEA	Total	CAS	CEA	Total
PP Population (N = 2307)	599	620	1219 (52.8%)	532	556	1088 (47.2%)
All Randomized Subjects (N = 2502)	668	653	1321 (52.8%)	594	587	1181 (47.2%)

The medical history of subjects in the CAS and the CEA arms were balanced in both the symptomatic and asymptomatic subgroups of the PP population, the primary analysis population.

D. Safety and Effectiveness Results

The Per-Protocol (PP) population was designated as the primary population for analysis of the primary endpoint and secondary endpoints. This population is composed of the subjects treated with either CAS or CEA as their randomized procedure by an approved study investigator.

1. Safety Results

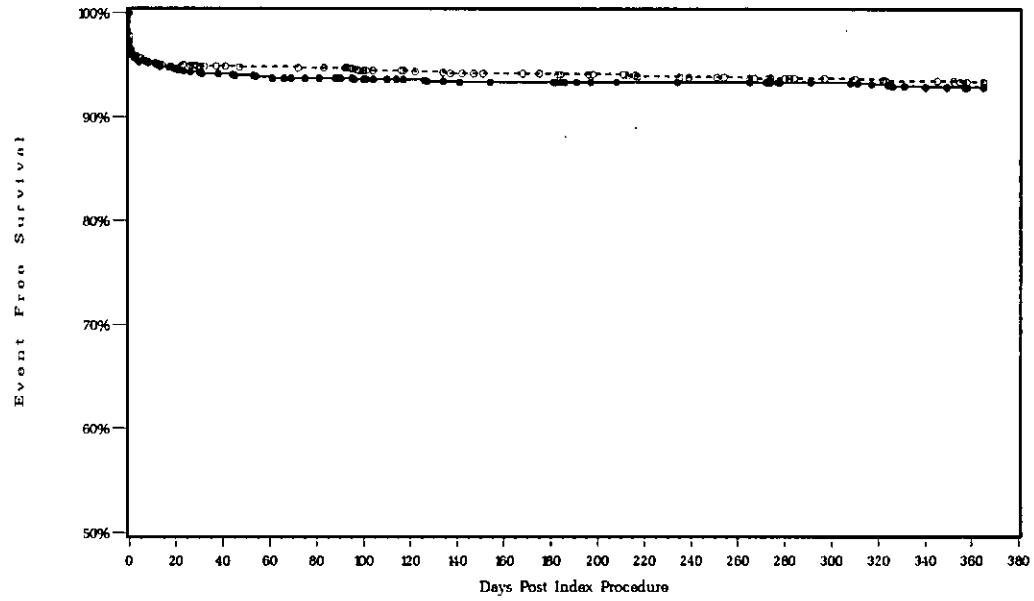
   The analysis of safety was based on the CREST randomized population treated with CAS or CEA, with follow-up data available for 96.0% (2365/2464) of subjects at 1 month and 90.3% (2140/2369) of subjects at 1 year post-procedure. Safety outcomes are presented in Tables 8 through 12 and Figures 4 through 9. Kaplan-Meier survival analysis of the primary endpoint through 365 days post-procedure for the PP analysis population is presented in Figure 4. Adverse effects are reported in Tables 13 to 15.

   CREST has met the primary endpoint of the trial with $p < 0.05$ in the PP population, the primary analysis population, as shown in Table 8. The observed difference between the primary endpoint event rates for CAS and CEA arms is 0.5% with a 95% upper confidence limit of 2.26% within the pre-specified non-inferiority margin of 2.6% ($p = 0.0245$). The primary endpoint was also met in all other analysis groups, e.g. the Per-Protocol (Adjusted) and ITT populations. CAS is statistically non-inferior to CEA when performed using the Acculink Carotid Stent System with the Accunet Embolic Protection System to treat standard surgical risk subjects with disease in the internal carotid artery.

Table 8: Summary of Non-inferiority Test Primary Endpoint Analyses

Analyses	One Year Primary Endpoint Event Rate (%) ± SE (%) (N)		Non-inferiority Test		
	CAS	CEA	Difference [95% CI]	Non-inferiority Test Margins	*p*-Value
Per-protocol	7.1% ± 0.77% (N = 1131)	6.6% ± 0.73% (N = 1176)	0.5% [-, 2.26%]	2.6%	0.0245
Per-protocol (Adjusted)	7.2% ± 0.77% (N = 1131)	6.5% ± 0.72% (N = 1176)	0.7% [-, 2.41%]	2.6%	0.0342
Intent-to-treat	7.0% ± 0.73% (N = 1259)	6.9% ± 0.73% (N = 1237)	0.1% [-, 1.80%]	2.6%	0.0077

Figure 4: Freedom from Primary Endpoint Events at 365 Days (PP Population)



Solid line. CAS Subjects (n= 1131)
Dashed line. CEA Subjects (n= 1176)

Days Post Index Procedure	0	(0, 2]	(2, 30]	(30, 180]	(180, 365]
CAS					
Subjects at Risk	1131	1094	1082	1062	1031
Subjects Censored	0	1	3	21	1026
Number of Events	37	11	17	10	5
% Event Free	96.7%	95.8%	94.2%	93.4%	92.9%
% Standard Error	0.5%	0.6%	0.7%	0.7%	0.8%
CEA					
Subjects at Risk	1176	1150	1127	1110	1083
Subjects Censored	0	1	5	19	1074
Number of Events	26	22	12	8	9
% Event Free	97.8%	95.9%	94.9%	94.2%	93.4%
% Standard Error	0.4%	0.6%	0.6%	0.7%	0.7%
Tests Between Groups	Test	Chi-Square	DF	p-value	
	Log-Rank	0.268	1	0.6047	
	Wilcoxon	0.304	1	0.5815	

Assessment of the Primary Endpoint for Symptomatic and Asymptomatic Subjects

For both symptomatic and asymptomatic subgroups, CREST has also met the endpoint with $p < 0.05$ in the pre-specified non-inferiority test for both the PP and ITT analysis populations as shown in Table 9. CAS is statistically non-inferior to CEA regardless of the subject symptomatic status when CAS is performed using the Acculink Carotid Stent System with the Accunet Embolic Protection System to treat standard surgical risk subjects with disease in the internal carotid artery.

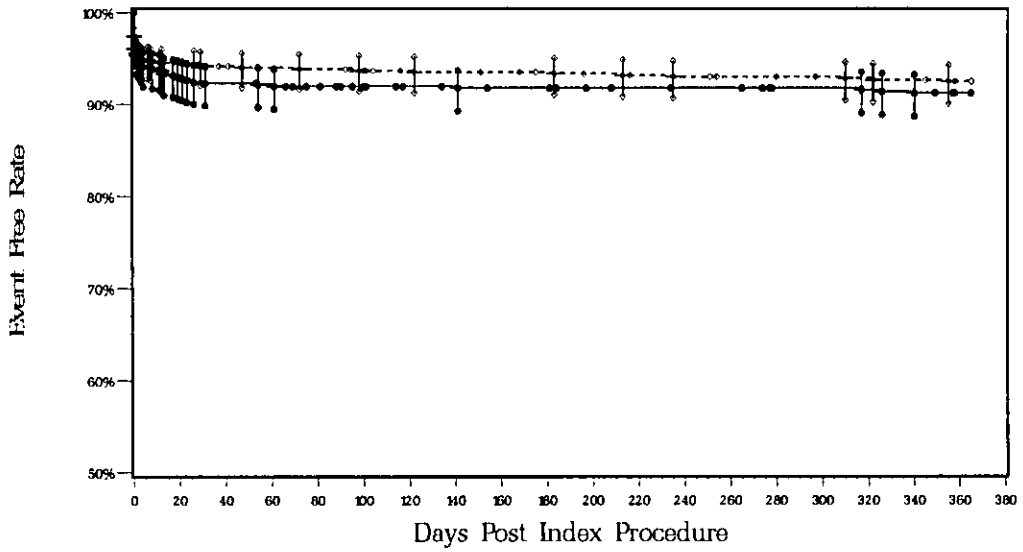
21

Table 9: Summary of Non-inferiority Tests by Symptomatic Status

Analyses	One Year Primary Endpoint Event Rate (%) ± SE (%) (N)		Non-inferiority Test		
	CAS	CEA	Difference [95% CI]	Non-inferiority Test Margins (N)	*p*-Value
PP -- Symptomatic	8.7% ± 1.16% (N = 599)	7.5% ± 1.06% (N = 620)	1.3% [-, 3.84%]	3.875% (N = 1219)	0.0477
PP -- Asymptomatic	5.3% ± 0.97% (N = 532)	5.6% ± 0.98% (N = 556)	-0.3% [-, 1.95%]	3.400% (N = 1088)	0.0035
ITT -- Symptomatic	8.5% ± 1.09% (N = 667)	8.0% ± 1.07% (N = 652)	0.6% [-, 3.08%]	3.775% (N = 1319)	0.0179
ITT -- Asymptomatic	5.3% ± 0.93% (N = 592)	5.7% ± 0.97% (N = 585)	-0.4% [-, 1.79%]	3.200% (N = 1177)	0.0035

The freedom from the estimated one-year composite primary endpoint event rates are 91.3% in the CAS arm and 92.5% in the CEA arm for symptomatic subjects. The Kaplan-Meier survival curves of CAS and CEA are comparable (see Figure 5 below).

Figure 5: CREST - SYMPTOMATIC CAS and CEA Subjects – Freedom from One-Year Composite Endpoint (PP Population)



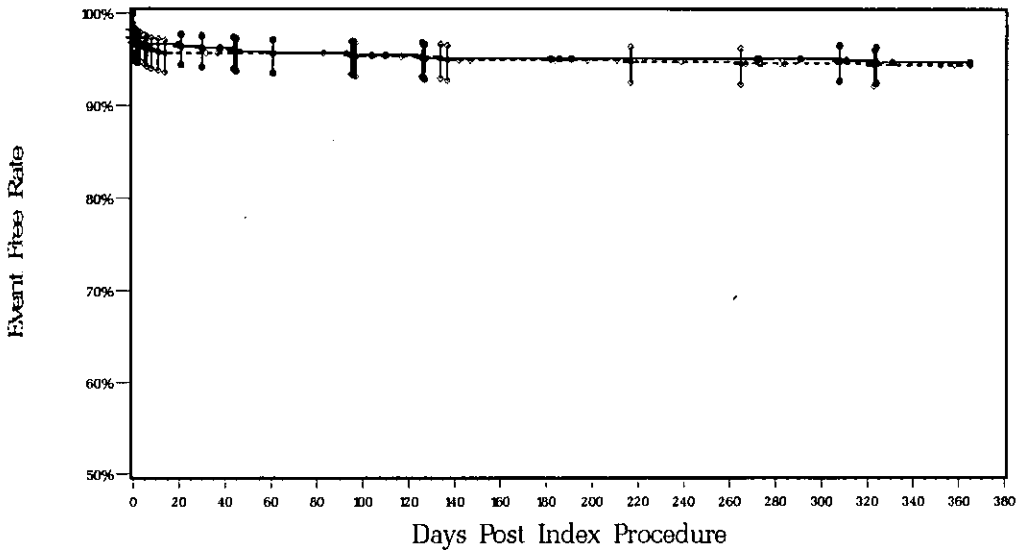
Solid line: CAS Subjects (n= 599)
Dashed line: CEA Subjects (n= 620)
Vertical bar: 95% Confidence Limit

Days Post Index Procedure	0	(0, 2]	(2, 30]	(30, 180]	(180, 365]
CAS					
Subjects at Risk	599	576	568	552	531
Subjects Censored	0	1	1	17	528
Number of Events	23	7	15	4	3
% Event Free	96.2%	95.0%	92.5%	91.8%	91.3%
% Standard Error	0.8%	0.9%	1.1%	1.1%	1.2%
CEA					
Subjects at Risk	620	604	589	579	563
Subjects Censored	0	0	5	12	557
Number of Events	16	15	5	4	6
% Event Free	97.4%	95.0%	94.2%	93.5%	92.5%
% Standard Error	0.6%	0.9%	0.9%	1.0%	1.1%
Tests Between Groups	Test	Chi-Square	DF	p-value	
	Log-Rank	0.685	1	0.4078	
	Wilcoxon	0.731	1	0.3926	

Note: Subjects at risk gives the number of subjects at risk of an event at the start of the interval, while subjects censored and number of events are the incremental counts of subjects censored or with events during the interval. The intervals are denoted as half-open bracket expression, where the start of interval '(' is exclusive and the end of the interval ']' is inclusive.

The freedom from the estimated one-year composite primary endpoint event rates are 94.7% in the CAS arm and 94.4% in the CEA arm for asymptomatic subjects. The Kaplan-Meier survival curves of CAS and CEA are comparable (see Figure 6 below).

Figure 6: CREST - ASYMPTOMATIC CAS and CEA Subjects – Freedom from One-Year Composite Endpoint (PP Population)



Solid line: CAS Subjects (n= 532)
Dashed line: CEA Subjects (n= 556)
Vertical bar: 95% Confidence Limit

Days Post Index Procedure	0	(0, 2]	(2, 30]	(30, 180]	(180, 365]
CAS					
Subjects at Risk	532	518	514	510	500
Subjects Censored	0	0	2	4	498
Number of Events	14	4	2	6	2
% Event Free	97.4%	96.6%	96.2%	95.1%	94.7%
% Standard Error	0.7%	0.8%	0.8%	0.9%	1.0%
CEA					
Subjects at Risk	556	546	538	531	520
Subjects Censored	0	1	0	7	517
Number of Events	10	7	7	4	3
% Event Free	98.2%	96.9%	95.7%	95.0%	94.4%
% Standard Error	0.6%	0.7%	0.9%	0.9%	1.0%
Tests Between Groups	Test	Chi-Square	DF	p-value	
	Log-Rank	0.049	1	0.8240	

	Wilcoxon	0.041	1	0.8390	

Note: Subjects at risk gives the number of subjects at risk of an event at the start of the interval, while subjects censored and number of events are the incremental counts of subjects censored or with events during the interval. The intervals are denoted as half-open bracket expression, where the start of interval '(' is exclusive and the end of the interval ']' is inclusive.

Assessment of DSMI at 30 days

Peri-procedural death, stroke and myocardial infarction (DSMI) comprise a secondary safety endpoint. CREST has met the DSMI endpoint of the trial with $p < 0.05$ in the PP population, the primary analysis population, as shown in Table 10. The observed difference between the DSMI event rates for CAS and CEA arms is 0.6% for PP population with a 95% upper confidence limit of 2.20% within the pre-specified non-inferiority margin of 2.3% ($p = 0.0401$). The DSMI endpoint was also met in the ITT population. CAS is statistically non-inferior to CEA when performed using the Acculink Carotid Stent System with the Accunet Embolic Protection System to treat standard surgical risk subjects with disease in the internal carotid artery.

Table 10: Summary of Non-inferiority Tests for Peri-procedural Events

Analyses[1]	Peri-procedural Events Event Rate (%) ± SE (%) (N)			Non-inferiority Test	
	CAS	CEA	Difference [95% CI]	Non-inferiority Test Margins	*p*-Value
Per-protocol	5.8% ± 0.69% (N = 1131)	5.1% ± 0.64% (N = 1176)	0.6% [-, 2.20%]	2.3%	0.0401
Intent-to-treat	5.8% ± 0.66% (N = 1259)	5.5% ± 0.65% (N = 1237)	0.3% [-, 1.83%]	2.3%	0.0155

The components of DSMI were evaluated separately and the results show that the stroke rate, driven predominantly by minor (non-major) strokes, is significantly higher in CAS and the MI rate is significantly higher in CEA as shown in Table 11. The stroke rate in CAS is 4.1% (46/1127), compared to 1.9% (22/1175) in the CEA arm. The MI rate in CAS is 2.0% (22/1127), compared to 3.4% (40/1175) in the CEA arm. Both of these differences in rates are statistically significant.

Table 11: DSMI Event Rates at 30 Days (PP Population – Non-Hierarchical Events)

Non-hierarchical Events	CAS N = 1131	CEA N = 1176	Total N = 2307	Difference [95% CI]
All Stroke [95% Conf. Interval]	4.1% (46/1127) [3.0%, 5.4%]	1.9% (22/1175) [1.2%, 2.8%]	3.0% (68/2302) [2.3%, 3.7%]	2.2% [0.8%, 3.6%]
Minor Stroke [95% Conf. Interval]	3.2% (36/1127) [2.2%, 4.4%]	1.5% (18/1175) [0.9%, 2.4%]	2.3% (54/2302) [1.8%, 3.0%]	1.7% [0.4%, 2.9%]
MI [95% Conf. Interval]	2.0% (22/1127) [1.2%, 2.9%]	3.4% (40/1175) [2.4%, 4.6%]	2.7% (62/2302) [2.1%, 3.4%]	-1.5% [-2.8%, -0.1%]
Death [95% Conf. Interval]	0.5% (6/1127) [0.2%, 1.2%]	0.3% (3/1175) [0.1%, 0.7%]	0.4% (9/2302) [0.2%, 0.7%]	0.3% Assumptions not met

The peri-procedural death and stroke rate of 5.9% (35/597) for CAS is within the AHA guideline of 6% death and stroke for treating symptomatic subjects. The

25

peri-procedural death and stroke rate of 2.5% (13/530) for CAS for asymptomatic subjects is within the AHA guideline of 3% death and stroke for treating asymptomatic subjects. These findings suggest that CAS is acceptable with respect to peri-procedural safety when treating symptomatic and asymptomatic subjects.

Analysis by Octogenarian Status

For the non-octogenarian subgroup, the composite endpoint rates are 6.7% in the CAS arm vs. 6.2% in the CEA arm in the PP population, and are 6.5% in the CAS arm vs. 6.5% in the CEA arm in the ITT population. Both analyses reach statistical significance with a p-value < 0.05% with a non-inferiority margin of 2.6%, as seen in Table 12. Therefore, CAS is non-inferior to CEA for treating non-octogenarian subjects.

Table 12: Non-inferiority Test on One-Year Composite Endpoint for Non-Octogenarian Subjects

Analyses	One Year Primary Endpoint Event Rate (%) ± SE (%) (N)		Non-inferiority Test		
	CAS	CEA	Difference [95% CI]	Non-inferiority Test Margins	p-Value
Per-protocol	6.7% ± 0.78% (N = 1025)	6.2% ± 0.74% (N = 1073)	0.5% [-, 2.24%]	2.6%	0.0238
Intent-to-treat	6.5% ± 0.74% (N = 1132)	6.5% ± 0.74% (N = 1124)	0.0% [-, 1.75%]	2.6%	0.0070

The 30-day DSMI rate is 5.5% (56/1021) in the CAS arm and 4.8% (51/1072) in the CEA arm in non-octogenarians and 8.5% (9/106) in the CAS arm and 8.7% (9/103) in the CEA arm in octogenarians. No significant difference is shown between the CAS and the CEA treatment arms for both the octogenarian and non-octogenarian subgroups.

Access Site Complications

For the 2403 subjects with at least one study procedure attempted, and based on the first attempted treatment, the rate of access site complications requiring treatment is 1.1% (13/1157) in the CAS arm and 3.5% (43/1246) in the CEA arm. There is a statistically significant difference between the rates of access site complications in the CAS and CEA arms.

Cranial Nerve Injury Unresolved at 1 and 6 months

For the 2403 subjects with at least one study procedure attempted, and based on the first attempted treatment, the data show that 5.2% (65/1246) of subjects had cranial nerve injury due to the CEA treatment. The cranial nerve injury was unresolved in 3.5% (44/1246) of CEA subjects at 1 month and in 2.0% (25/1246) of CEA subjects at 6 months post-procedure. Cranial nerve injury did not occur in subjects treated with CAS.

Adverse events that occurred in the PMA clinical study:

Tables 13 through 15 present the adverse events reported for patients in the CREST study during the time points indicated.

There were 213 deaths reported of which 112 were in the CAS arm and 101 in the CEA arm as presented in Table 16. In the CAS arm, 8 deaths occurred in the first 30 days after the procedure or randomization for those subjects without a study procedure, 4 are related to stroke, 2 are related to cardiac causes, 1 is related to bleeding and 1 is related to sepsis. In the CEA arm, 4 deaths occurred in the first 30 days and all 4 were related to stroke.

Table 13: All Reported Non-Primary Endpoint Adverse Events within 30 Days following the Study Procedure (All Randomized Subjects)

Category	Subcategory	First Attempted CAS [1] N = 1156			First Attempted CEA [1] N = 1246		
		Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE	Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE
Access Site Complication Not Requiring Treatment		0.1% (1/1156)	4.2% (49/1156)	4.3% (50/1156)	0.2% (2/1246)	5.7% (71/1246)	5.9% (73/1246)
	Bleeding	0.0% (0/1156)	1.6% (18/1156)	1.6% (18/1156)	0.0% (0/1246)	0.3% (4/1246)	0.3% (4/1246)
	Fistula/Pseudoaneurysm/Dissection	0.0% (0/1156)	0.3% (3/1156)	0.3% (3/1156)	0.0% (0/1246)	0.0% (0/1246)	0.0% (0/1246)
	Hematoma	0.1% (1/1156)	2.3% (27/1156)	2.4% (28/1156)	0.1% (1/1246)	1.6% (20/1246)	1.7% (21/1246)
	Incision Complication	0.0% (0/1156)	0.1% (1/1156)	0.1% (1/1156)	0.1% (1/1246)	2.1% (26/1246)	2.2% (27/1246)
	Pain	0.0% (0/1156)	0.5% (6/1156)	0.5% (6/1156)	0.0% (0/1246)	2.1% (26/1246)	2.1% (26/1246)
Access Site Complication Requiring Treatment		0.9% (10/1156)	0.3% (4/1156)	1.1% (13/1156)	2.0% (25/1246)	1.4% (18/1246)	3.4% (42/1246)
	Bleeding	0.3% (4/1156)	0.1% (1/1156)	0.4% (5/1156)	0.2% (3/1246)	0.2% (2/1246)	0.4% (5/1246)
	Hematoma	0.3% (3/1156)	0.2% (2/1156)	0.4% (5/1156)	1.3% (16/1246)	0.4% (5/1246)	1.7% (21/1246)
	Incision Complication	0.0% (0/1156)	0.0% (0/1156)	0.0% (0/1156)	0.2% (3/1246)	0.0% (0/1246)	0.2% (3/1246)
	Infection	0.0% (0/1156)	0.0% (0/1156)	0.0% (0/1156)	0.1% (1/1246)	0.5% (6/1246)	0.6% (7/1246)
	Occlusion	0.2% (2/1156)	0.1% (1/1156)	0.3% (3/1156)	0.0% (0/1246)	0.0% (0/1246)	0.0% (0/1246)
	Pain	0.0% (0/1156)	0.0% (0/1156)	0.0% (0/1156)	0.1% (1/1246)	0.3% (4/1246)	0.4% (5/1246)
	Pseudoaneurysm	0.1% (1/1156)	0.0% (0/1156)	0.1% (1/1156)	0.1% (1/1246)	0.1% (1/1246)	0.2% (2/1246)

[1] Subjects first attempted procedure was CAS or CEA. The denominator for each treatment arm is based on the first treatment attempted so that CAS subjects crossed over to CEA after the procedure was attempted are counted in CAS.

Table 13 (continued)

Category	Subcategory	First Attempted CAS [1] N = 1156			First Attempted CEA [1] N = 1246		
		Subjects with Serious AEs	Subjects with Non-serious AEs[2]	Subjects with any AE	Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE
Allergic Reaction		0.3% (4/1156)	0.8% (9/1156)	1.1% (13/1156)	0.2% (2/1246)	0.3% (4/1246)	0.5% (6/1246)
Bleeding		0.2% (2/1156)	0.7% (8/1156)	0.9% (10/1156)	0.2% (3/1246)	0.3% (4/1246)	0.6% (7/1246)
	Epistaxis	0.0% (0/1156)	0.1% (1/1156)	0.1% (1/1156)	0.0% (0/1246)	0.0% (0/1246)	0.0% (0/1246)
	GI	0.1% (1/1156)	0.3% (4/1156)	0.4% (5/1156)	0.2% (2/1246)	0.1% (1/1246)	0.2% (3/1246)
	Other	0.1% (1/1156)	0.3% (3/1156)	0.3% (4/1156)	0.1% (1/1246)	0.2% (3/1246)	0.3% (4/1246)
Blood Dyscrasia		0.4% (5/1156)	0.6% (7/1156)	1.0% (11/1156)	0.3% (4/1246)	0.6% (7/1246)	0.9% (11/1246)
Cancer		0.3% (3/1156)	0.1% (1/1156)	0.3% (4/1156)	0.3% (4/1246)	0.1% (1/1246)	0.4% (5/1246)
Cardiac		1.1% (13/1156)	4.6% (53/1156)	5.6% (65/1156)	1.8% (22/1246)	5.3% (66/1246)	6.8% (85/1246)
	Abnormal Lab Test	0.0% (0/1156)	2.9% (34/1156)	2.9% (34/1156)	0.0% (0/1246)	3.5% (44/1246)	3.5% (44/1246)
	Arrhythmia	0.3% (4/1156)	0.4% (5/1156)	0.8% (9/1156)	0.6% (8/1246)	0.9% (11/1246)	1.5% (19/1246)
	Cardiac Arrest	0.1% (1/1156)	0.0% (0/1156)	0.1% (1/1156)	0.0% (0/1246)	0.0% (0/1246)	0.0% (0/1246)
	Congestive Heart Failure	0.2% (2/1156)	0.1% (1/1156)	0.3% (3/1156)	0.3% (4/1246)	0.1% (1/1246)	0.4% (5/1246)
	Coronary Artery Disease	0.5% (6/1156)	1.0% (12/1156)	1.6% (18/1156)	0.8% (10/1246)	0.9% (11/1246)	1.7% (21/1246)
	Pulmonary Hypertension	0.0% (0/1156)	0.1% (1/1156)	0.1% (1/1156)	0.0% (0/1246)	0.0% (0/1246)	0.0% (0/1246)
	Structural Heart Disease	0.0% (0/1156)	0.1% (1/1156)	0.1% (1/1156)	0.0% (0/1246)	0.0% (0/1246)	0.0% (0/1246)

Table 13 (continued)

Category	Subcategory	First Attempted CAS [1] N = 1156			First Attempted CEA [1] N = 1246		
		Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE	Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE
Gastrointestinal		0.6% (7/1156)	0.9% (10/1156)	1.4% (16/1156)	0.3% (4/1246)	0.7% (9/1246)	1.0% (13/1246)
Genitourinary		0.3% (3/1156)	0.7% (8/1156)	1.0% (11/1156)	0.2% (2/1246)	0.7% (9/1246)	0.9% (11/1246)
Hemodynamic		0.3% (4/1156)	0.2% (2/1156)	0.5% (6/1156)	0.2% (3/1246)	1.2% (15/1246)	1.4% (18/1246)
	Hypertension	0.0% (0/1156)	0.0% (0/1156)	0.0% (0/1156)	0.0% (0/1246)	0.1% (1/1246)	0.1% (1/1246)
	Presyncope / Syncope	0.3% (4/1156)	0.2% (2/1156)	0.5% (6/1156)	0.2% (3/1246)	1.1% (14/1246)	1.4% (17/1246)
Infection		1.3% (15/1156)	0.9% (10/1156)	2.1% (24/1156)	0.8% (10/1246)	1.3% (16/1246)	2.1% (26/1246)
Mental Health Related		0.2% (2/1156)	0.5% (6/1156)	0.7% (8/1156)	0.1% (1/1246)	0.6% (8/1246)	0.7% (9/1246)
Metabolic		0.1% (1/1156)	0.8% (9/1156)	0.9% (10/1156)	0.2% (2/1246)	1.0% (13/1246)	1.2% (15/1246)
Miscellaneous		0.0% (0/1156)	1.6% (19/1156)	1.6% (19/1156)	0.0% (0/1246)	2.1% (26/1246)	2.1% (26/1246)
Musculoskeletal		0.2% (2/1156)	1.5% (17/1156)	1.6% (19/1156)	0.5% (6/1246)	1.3% (16/1246)	1.7% (21/1246)
Neurologic Other Than Stroke		0.8% (9/1156)	3.5% (41/1156)	4.2% (49/1156)	0.9% (11/1246)	3.5% (43/1246)	4.3% (54/1246)
	Amaurosis Fugax	0.0% (0/1156)	0.5% (6/1156)	0.5% (6/1156)	0.1% (1/1246)	0.6% (7/1246)	0.6% (8/1246)
	Confusion	0.1% (1/1156)	0.1% (1/1156)	0.2% (2/1156)	0.0% (0/1246)	0.2% (2/1246)	0.2% (2/1246)
	Dementia	0.0% (0/1156)	0.1% (1/1156)	0.1% (1/1156)	0.0% (0/1246)	0.0% (0/1246)	0.0% (0/1246)
	Hyperperfusion Syndrome	0.0% (0/1156)	0.0% (0/1156)	0.0% (0/1156)	0.1% (1/1246)	0.0% (0/1246)	0.1% (1/1246)
	Migraine	0.0% (0/1156)	0.1% (1/1156)	0.1% (1/1156)	0.0% (0/1246)	0.0% (0/1246)	0.0% (0/1246)
	Neurologic Other	0.0% (0/1156)	0.4% (5/1156)	0.4% (5/1156)	0.0% (0/1246)	0.6% (8/1246)	0.6% (8/1246)
	Peripheral Neuropathy	0.0% (0/1156)	0.2% (2/1156)	0.2% (2/1156)	0.1% (1/1246)	0.1% (1/1246)	0.2% (2/1246)

Table 13 (continued)

Category	Subcategory	First Attempted CAS [a] N = 1156			First Attempted CEA [a] N = 1246		
		Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE	Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE
	Seizure	0.2% (2/1156)	0.0% (0/1156)	0.2% (2/1156)	0.2% (3/1246)	0.1% (1/1246)	0.3% (4/1246)
	Sensory Deficit	0.0% (0/1156)	0.1% (1/1156)	0.1% (1/1156)	0.0% (0/1246)	0.3% (4/1246)	0.3% (4/1246)
	Speech Disturbance	0.1% (1/1156)	0.0% (0/1156)	0.1% (1/1156)	0.0% (0/1246)	0.0% (0/1246)	0.0% (0/1246)
	Subdural Hematoma	0.0% (0/1156)	0.0% (0/1156)	0.0% (0/1156)	0.1% (1/1246)	0.0% (0/1246)	0.1% (1/1246)
	TIA	0.4% (5/1156)	1.8% (21/1156)	2.2% (25/1156)	0.3% (4/1246)	1.2% (15/1246)	1.5% (19/1246)
	Vertigo	0.0% (0/1156)	0.0% (0/1156)	0.0% (0/1156)	0.0% (0/1246)	0.1% (1/1246)	0.1% (1/1246)
	Visual Disturbance	0.0% (0/1156)	0.3% (3/1156)	0.3% (3/1156)	0.0% (0/1246)	0.3% (4/1246)	0.3% (4/1246)
Procedure Related		6.3% (73/1156)	25.7% (297/1156)	29.8% (345/1156)	4.7% (58/1246)	27.4% (341/1246)	31.1% (387/1246)
	Anesthesia / Procedural Medication Related	0.2% (2/1156)	1.2% (14/1156)	1.4% (16/1156)	0.3% (4/1246)	3.5% (43/1246)	3.8% (47/1246)
	Arrhythmia	0.7% (8/1156)	3.2% (37/1156)	3.9% (45/1156)	0.2% (2/1246)	0.8% (10/1246)	1.0% (12/1246)
	Bleeding	0.8% (9/1156)	0.5% (6/1156)	1.3% (15/1156)	1.0% (13/1246)	0.8% (10/1246)	1.8% (23/1246)
	Cranial Nerve Injury	0.0% (0/1156)	0.0% (0/1156)	0.0% (0/1156)	0.4% (5/1246)	4.6% (57/1246)	5.0% (62/1246)
	Fever	0.0% (0/1156)	0.1% (1/1156)	0.1% (1/1156)	0.0% (0/1246)	0.1% (1/1246)	0.1% (1/1246)
	Fluid Over Load	0.1% (1/1156)	0.0% (0/1156)	0.1% (1/1156)	0.0% (0/1246)	0.1% (1/1246)	0.1% (1/1246)
	Graft Infection	0.0% (0/1156)	0.0% (0/1156)	0.0% (0/1156)	0.1% (1/1246)	0.0% (0/1246)	0.1% (1/1246)
	Headache	0.0% (0/1156)	1.6% (19/1156)	1.6% (19/1156)	0.4% (5/1246)	1.4% (18/1246)	1.8% (23/1246)
	Heparin Induced Thrombocytopenia	0.0% (0/1156)	0.1% (1/1156)	0.1% (1/1156)	0.0% (0/1246)	0.0% (0/1246)	0.0% (0/1246)
	Horners Syndrome	0.0% (0/1156)	0.0% (0/1156)	0.0% (0/1156)	0.0% (0/1246)	0.2% (2/1246)	0.2% (2/1246)

Table 13 (continued)

Category	Subcategory	First Attempted CAS [1] N = 1156			First Attempted CEA [1] N = 1246		
		Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE	Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE
	Hypertension	0.4% (5/1156)	5.2% (60/1156)	5.6% (65/1156)	1.4% (17/1246)	11.7% (146/1246)	13.1% (163/1246)
	Hypoperfusion	0.0% (0/1156)	0.0% (0/1156)	0.0% (0/1156)	0.1% (1/1246)	0.0% (0/1246)	0.1% (1/1246)
	Hypotension	4.5% (52/1156)	16.9% (195/1156)	21.4% (247/1156)	1.0% (12/1246)	8.7% (108/1246)	9.6% (120/1246)
	Pain	0.0% (0/1156)	1.1% (13/1156)	1.1% (13/1156)	0.0% (0/1246)	2.4% (30/1246)	2.4% (30/1246)
	Spasm	0.0% (0/1156)	0.3% (4/1156)	0.3% (4/1156)	0.0% (0/1246)	0.0% (0/1246)	0.0% (0/1246)
	Urinary Retention	0.2% (2/1156)	0.5% (6/1156)	0.7% (8/1156)	0.2% (2/1246)	1.4% (18/1246)	1.6% (20/1246)
	Vessel Trauma	0.0% (0/1156)	0.2% (2/1156)	0.2% (2/1156)	0.0% (0/1246)	0.2% (2/1246)	0.2% (2/1246)
Respiratory		0.6% (7/1156)	0.3% (4/1156)	1.0% (11/1156)	0.6% (7/1246)	1.4% (18/1246)	2.0% (25/1246)
Trauma		0.0% (0/1156)	0.1% (1/1156)	0.1% (1/1156)	0.1% (1/1246)	0.4% (5/1246)	0.5% (6/1246)
Unknown AE		0.2% (2/1156)	0.0% (0/1156)	0.2% (2/1156)	0.1% (1/1246)	0.0% (0/1246)	0.1% (1/1246)
Vascular		0.9% (10/1156)	0.4% (5/1156)	1.3% (15/1156)	0.6% (7/1246)	0.7% (9/1246)	1.3% (16/1246)
	Aneurysm	0.1% (1/1156)	0.0% (0/1156)	0.1% (1/1156)	0.0% (0/1246)	0.2% (2/1246)	0.2% (2/1246)
	Carotid Artery Disease	0.0% (0/1156)	0.0% (0/1156)	0.0% (0/1156)	0.0% (0/1246)	0.1% (1/1246)	0.1% (1/1246)
	Contralateral Stenosis	0.1% (1/1156)	0.1% (1/1156)	0.2% (2/1156)	0.2% (2/1246)	0.1% (1/1246)	0.2% (3/1246)
	Deep Vein Thrombosis	0.0% (0/1156)	0.1% (1/1156)	0.1% (1/1156)	0.0% (0/1246)	0.0% (0/1246)	0.0% (0/1246)
	Occlusion	0.1% (1/1156)	0.0% (0/1156)	0.1% (1/1156)	0.1% (1/1246)	0.1% (1/1246)	0.2% (2/1246)
	Peripheral Vascular Disease	0.5% (6/1156)	0.3% (3/1156)	0.8% (9/1156)	0.0% (0/1246)	0.2% (3/1246)	0.2% (3/1246)
	Renal Vascular Disease	0.1% (1/1156)	0.0% (0/1156)	0.1% (1/1156)	0.0% (0/1246)	0.0% (0/1246)	0.0% (0/1246)

Table 13 (continued)

Category	Subcategory	First Attempted CAS [1] N = 1156			First Attempted CEA [1] N = 1246		
		Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE	Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE
	Target Lesion Restenosis	0.0% (0/1156)	0.0% (0/1156)	0.0% (0/1156)	0.1% (1/1246)	0.1% (1/1246)	0.2% (2/1246)
	Target Lesion Thrombosis	0.0% (0/1156)	0.0% (0/1156)	0.0% (0/1156)	0.2% (2/1246)	0.0% (0/1246)	0.2% (2/1246)
	Thrombosis	0.0% (0/1156)	0.0% (0/1156)	0.0% (0/1156)	0.1% (1/1246)	0.0% (0/1246)	0.1% (1/1246)

Table 14: All Reported Non-Primary Endpoint Adverse Events between 31 and 365 Days following the Study Procedure (All Randomized Subjects)

Category	Subcategory	First Attempted CAS [1] N = 1145			First Attempted CEA [1] N = 1230		
		Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE	Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE
Access Site Complication Not Requiring Treatment	Incision Complication	0.0% (0/1145)	0.0% (0/1145)	0.0% (0/1145)	0.0% (0/1230)	0.1% (1/1230)	0.1% (1/1230)
Access Site Complication Requiring Treatment	Hematoma	0.0% (0/1145)	0.0% (0/1145)	0.0% (0/1145)	0.1% (1/1230)	0.0% (0/1230)	0.1% (1/1230)
Allergic Reaction		0.0% (0/1145)	0.1% (1/1145)	0.1% (1/1145)	0.2% (3/1230)	0.2% (2/1230)	0.4% (5/1230)
Bleeding		1.4% (16/1145)	0.7% (8/1145)	2.1% (24/1145)	1.0% (12/1230)	1.1% (13/1230)	1.9% (23/1230)
	Epistaxis	0.0% (0/1145)	0.3% (4/1145)	0.3% (4/1145)	0.0% (0/1230)	0.1% (1/1230)	0.1% (1/1230)
	GI	1.2% (14/1145)	0.3% (3/1145)	1.5% (17/1145)	0.7% (9/1230)	0.3% (4/1230)	0.9% (11/1230)
	Other	0.2% (2/1145)	0.1% (1/1145)	0.3% (3/1145)	0.2% (3/1230)	0.7% (8/1230)	0.9% (11/1230)
Blood Dyscrasia		0.6% (7/1145)	0.6% (7/1145)	1.2% (14/1145)	0.5% (6/1230)	0.3% (4/1230)	0.8% (10/1230)
Cancer		1.5% (17/1145)	0.2% (2/1145)	1.7% (19/1145)	1.2% (15/1230)	0.2% (2/1230)	1.4% (17/1230)
Cardiac		4.5% (52/1145)	2.6% (30/1145)	6.8% (78/1145)	4.7% (58/1230)	3.2% (39/1230)	7.1% (87/1230)
	Abnormal Lab Test	0.1% (1/1145)	0.6% (7/1145)	0.6% (7/1145)	0.1% (1/1230)	0.5% (6/1230)	0.6% (7/1230)
	Arrhythmia	0.6% (7/1145)	1.1% (13/1145)	1.7% (20/1145)	1.4% (17/1230)	1.1% (14/1230)	2.3% (28/1230)
	Cardiac Arrest	0.6% (7/1145)	0.0% (0/1145)	0.6% (7/1145)	0.1% (1/1230)	0.0% (0/1230)	0.1% (1/1230)
	Congestive Heart Failure	0.4% (5/1145)	0.1% (1/1145)	0.5% (6/1145)	0.6% (7/1230)	0.2% (2/1230)	0.7% (9/1230)
	Coronary Artery Disease	3.1% (36/1145)	1.1% (13/1145)	4.1% (47/1145)	3.0% (37/1230)	1.5% (18/1230)	4.0% (49/1230)
	Structural Heart Disease	0.0% (0/1145)	0.0% (0/1145)	0.0% (0/1145)	0.1% (1/1230)	0.0% (0/1230)	0.1% (1/1230)

[1] Subjects first attempted study procedure was CAS or CEA and the subjects were in the study beyond 30 days post procedure.

Table 14 (continued)

Category	Subcategory	First Attempted CAS [1] N = 1145			First Attempted CEA [1] N = 1230		
		Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE	Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE
Gastrointestinal		1.5% (17/1145)	1.6% (18/1145)	2.9% (33/1145)	1.1% (14/1230)	1.1% (14/1230)	2.3% (28/1230)
Genitourinary		1.8% (21/1145)	0.3% (3/1145)	2.1% (24/1145)	1.1% (14/1230)	1.1% (14/1230)	2.2% (27/1230)
Hemodynamic		1.7% (19/1145)	2.5% (29/1145)	4.0% (46/1145)	1.6% (20/1230)	1.9% (23/1230)	3.3% (41/1230)
	Hypertension	0.5% (6/1145)	0.9% (10/1145)	1.3% (15/1145)	0.5% (6/1230)	0.5% (6/1230)	1.0% (12/1230)
	Hypotension	0.3% (3/1145)	0.3% (4/1145)	0.6% (7/1145)	0.3% (4/1230)	0.6% (7/1230)	0.9% (11/1230)
	Presyncope/Syncope	0.9% (10/1145)	1.4% (16/1145)	2.2% (25/1145)	0.9% (11/1230)	0.8% (10/1230)	1.7% (21/1230)
Infection		1.7% (19/1145)	1.9% (22/1145)	3.5% (40/1145)	1.9% (23/1230)	2.0% (24/1230)	3.4% (42/1230)
Mental Health Related		0.3% (4/1145)	0.3% (4/1145)	0.7% (8/1145)	0.2% (3/1230)	0.6% (7/1230)	0.8% (10/1230)
Metabolic		0.8% (9/1145)	1.4% (16/1145)	2.2% (25/1145)	0.5% (6/1230)	0.7% (9/1230)	1.1% (14/1230)
Miscellaneous		0.5% (6/1145)	2.8% (32/1145)	3.3% (38/1145)	0.3% (4/1230)	2.8% (34/1230)	3.1% (38/1230)
Musculoskeletal		1.5% (17/1145)	2.6% (30/1145)	4.0% (46/1145)	1.1% (13/1230)	2.6% (32/1230)	3.5% (43/1230)
Myocardial Infarction[2]		1.0% (12/1145)	0.0% (0/1145)	1.0% (12/1145)	1.1% (13/1230)	0.0% (0/1230)	1.1% (13/1230)

[2] The MI or stroke in the table are not primary endpoint events based on the definition of one year primary endpoint.

Table 14 (continued)

Category	Subcategory	First Attempted CAS [1] N = 1145			First Attempted CEA [1] N = 1230		
		Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE	Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE
Neurologic Other Than Stroke		2.5% (29/1145)	3.8% (44/1145)	6.2% (71/1145)	2.4% (30/1230)	4.4% (54/1230)	6.5% (80/1230)
	Amaurosis Fugax	0.3% (3/1145)	0.4% (5/1145)	0.7% (8/1145)	0.1% (1/1230)	0.3% (4/1230)	0.4% (5/1230)
	Confusion	0.0% (0/1145)	0.2% (2/1145)	0.2% (2/1145)	0.0% (0/1230)	0.0% (0/1230)	0.0% (0/1230)
	Contra-Lateral Cranial Nerve Injury	0.0% (0/1145)	0.1% (1/1145)	0.1% (1/1145)	0.0% (0/1230)	0.1% (1/1230)	0.1% (1/1230)
	Cranial Nerve Injury	0.0% (0/1145)	0.1% (1/1145)	0.1% (1/1145)	0.0% (0/1230)	0.2% (2/1230)	0.2% (2/1230)
	Dementia	0.0% (0/1145)	0.0% (0/1145)	0.0% (0/1145)	0.0% (0/1230)	0.2% (2/1230)	0.2% (2/1230)
	Migraine	0.2% (2/1145)	0.1% (1/1145)	0.3% (3/1145)	0.0% (0/1230)	0.2% (3/1230)	0.2% (3/1230)
	Neurologic Other	0.1% (1/1145)	0.3% (4/1145)	0.4% (5/1145)	0.2% (3/1230)	1.6% (20/1230)	1.9% (23/1230)
	Peripheral Neuropathy	0.0% (0/1145)	0.0% (0/1145)	0.0% (0/1145)	0.1% (1/1230)	0.2% (2/1230)	0.2% (3/1230)
	Seizure	0.3% (4/1145)	0.3% (4/1145)	0.7% (8/1145)	0.2% (3/1230)	0.0% (0/1230)	0.2% (3/1230)
	Sensory Deficit	0.0% (0/1145)	0.3% (3/1145)	0.3% (3/1145)	0.1% (1/1230)	0.3% (4/1230)	0.4% (5/1230)
	Speech Disturbance	0.2% (2/1145)	0.0% (0/1145)	0.2% (2/1145)	0.0% (0/1230)	0.1% (1/1230)	0.1% (1/1230)
	Subdural Hematoma	0.0% (0/1145)	0.0% (0/1145)	0.0% (0/1145)	0.1% (1/1230)	0.0% (0/1230)	0.1% (1/1230)
	TIA	1.4% (16/1145)	1.2% (14/1145)	2.5% (29/1145)	1.5% (18/1230)	1.0% (12/1230)	2.4% (29/1230)
	Vertigo	0.0% (0/1145)	0.3% (3/1145)	0.3% (3/1145)	0.1% (1/1230)	0.3% (4/1230)	0.4% (5/1230)
	Visual Disturbance	0.2% (2/1145)	0.6% (7/1145)	0.8% (9/1145)	0.1% (1/1230)	0.3% (4/1230)	0.4% (5/1230)

Table 14 (continued)

Category	Subcategory	First Attempted CAS [1] N = 1145			First Attempted CEA [1] N = 1230		
		Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE	Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE
Procedure Related	Cranial Nerve Injury	0.0% (0/1145)	0.0% (0/1145)	0.0% (0/1145)	0.0% (0/1230)	0.2% (3/1230)	0.2% (3/1230)
Respiratory		1.7% (19/1145)	1.0% (12/1145)	2.6% (30/1145)	1.4% (17/1230)	0.7% (8/1230)	2.0% (25/1230)
Stroke[2]		0.6% (7/1145)	0.0% (0/1145)	0.6% (7/1145)	0.5% (6/1230)	0.0% (0/1230)	0.5% (6/1230)
	Cerebral Hemorrhage, Non-Ipsilateral	0.0% (0/1145)	0.0% (0/1145)	0.0% (0/1145)	0.1% (1/1230)	0.0% (0/1230)	0.1% (1/1230)
	Ischemic, Non-Ipsilateral	0.6% (7/1145)	0.0% (0/1145)	0.6% (7/1145)	0.4% (5/1230)	0.0% (0/1230)	0.4% (5/1230)
Trauma		0.2% (2/1145)	0.4% (5/1145)	0.6% (7/1145)	1.1% (14/1230)	0.4% (5/1230)	1.5% (19/1230)
Unknown AE		0.3% (4/1145)	0.0% (0/1145)	0.3% (4/1145)	0.3% (4/1230)	0.1% (1/1230)	0.4% (5/1230)
Vascular		7.4% (85/1145)	0.8% (9/1145)	8.2% (94/1145)	6.4% (79/1230)	1.5% (19/1230)	7.6% (93/1230)
	Aneurysm	0.1% (1/1145)	0.0% (0/1145)	0.1% (1/1145)	0.2% (2/1230)	0.0% (0/1230)	0.2% (2/1230)
	Carotid Artery Disease	0.0% (0/1145)	0.0% (0/1145)	0.0% (0/1145)	0.1% (1/1230)	0.0% (0/1230)	0.1% (1/1230)
	Cerebral Malformation	0.1% (1/1145)	0.0% (0/1145)	0.1% (1/1145)	0.0% (0/1230)	0.0% (0/1230)	0.0% (0/1230)
	Contralateral Stenosis	2.1% (24/1145)	0.0% (0/1145)	2.1% (24/1145)	3.5% (43/1230)	0.2% (2/1230)	3.6% (44/1230)
	Deep Vein Thrombosis	0.0% (0/1145)	0.0% (0/1145)	0.0% (0/1145)	0.2% (2/1230)	0.0% (0/1230)	0.2% (2/1230)
	Fistula/Pseudoaneurysm/ Dissection	0.1% (1/1145)	0.0% (0/1145)	0.1% (1/1145)	0.0% (0/1230)	0.1% (1/1230)	0.1% (1/1230)
	Peripheral Vascular Disease	2.7% (31/1145)	0.3% (4/1145)	3.1% (35/1145)	0.9% (11/1230)	0.9% (11/1230)	1.6% (20/1230)
	Renal Vascular Disease	0.5% (6/1145)	0.0% (0/1145)	0.5% (6/1145)	0.3% (4/1230)	0.0% (0/1230)	0.3% (4/1230)
	Target Lesion Restenosis	1.8% (21/1145)	0.4% (5/1145)	2.3% (26/1145)	1.6% (20/1230)	0.4% (5/1230)	2.0% (24/1230)

[2] The MI or stroke in the table are not primary endpoint events based on the definition of one year primary endpoint.

Table 14 (continued)

Category	Subcategory	First Attempted CAS [1] N = 1145			First Attempted CEA [1] N = 1230		
		Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE	Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE
	Target Lesion Thrombosis	0.1% (1/1145)	0.0% (0/1145)	0.1% (1/1145)	0.0% (0/1230)	0.0% (0/1230)	0.0% (0/1230)
	Thrombosis	0.1% (1/1145)	0.0% (0/1145)	0.1% (1/1145)	0.0% (0/1230)	0.0% (0/1230)	0.0% (0/1230)

Table 15: All Reported Non-Primary Endpoint Adverse Events after 365 Days Post Study Procedure (All Randomized Subjects)

Category	Subcategory	First Attempted CAS [1] N = 1092			First Attempted CEA [1] N = 1175		
		Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE	Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE
Allergic Reaction		0	7	7	1	3	4
Bleeding		17	10	27	27	8	35
	Epistaxis	0	1	1	0	0	0
	GI	12	2	14	20	2	22
	Other	5	7	12	7	6	13
Blood Dyscrasia		14	10	23	10	9	18
Cancer		33	9	40	31	6	37
Cardiac		104	29	121	114	37	138
	Abnormal Lab Test	2	0	2	2	0	2
	Arrhythmia	15	15	28	25	24	48
	Cardiac Arrest	8	0	8	12	0	12
	Congestive Heart Failure	14	3	17	21	5	26
	Coronary Artery Disease	71	13	80	64	11	71
	Effusion	0	0	0	1	0	1

[1] Subjects first attempted study procedure was CAS or CEA and the subjects were in the study beyond 365 days post procedure.

Table 15 (continued)

Category	Subcategory	First Attempted CAS [1] N = 1092			First Attempted CEA [1] N = 1175		
		Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE	Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE
	Pulmonary Hypertension	0	0	0	1	0	1
	Structural Heart Disease	4	0	4	1	1	2
Gastrointestinal		31	20	44	27	19	41
Genitourinary		18	8	25	24	10	33
Hemodynamic		25	25	46	21	28	47
	Hypertension	5	6	10	6	11	16
	Hypotension	10	6	15	4	6	10
	Presyncope/Syncope	11	13	22	14	11	24
Infection		34	22	52	30	25	51
Mental Health Related		4	5	9	5	4	9
Metabolic		14	15	27	10	11	20
Miscellaneous		2	31	33	3	32	34
Musculoskeletal		32	35	61	33	37	68
Myocardial Infarction[2]		25	0	25	34	0	34

[2] The MI or stroke in the table are not primary endpoint events based on the definition of one year primary endpoint.

Table 15 (continued)

Category	Subcategory	First Attempted CAS [1] N = 1092			First Attempted CEA [1] N = 1175		
		Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE	Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE
Neurologic Other Than Stroke		44	59	96	34	62	92
	Amaurosis Fugax	9	4	12	1	7	8
	Confusion	1	3	4	1	1	2
	Cranial Nerve Injury	0	2	2	0	0	0
	Dementia	3	0	3	1	4	5
	Migraine	2	1	3	0	1	1
	Neurologic Other	0	10	10	1	13	14
	Peripheral Neuropathy	0	0	0	0	8	8
	Seizure	3	0	3	5	1	6
	Sensory Deficit	0	3	3	0	4	4
	Speech Disturbance	3	4	7	0	1	1
	Subdural Hematoma	0	0	0	1	0	1
	TIA	23	30	51	21	20	40
	Vertigo	3	1	4	2	3	4
	Visual Disturbance	1	5	6	2	5	7
Respiratory		28	8	34	31	11	40

Table 15 (continued)

Category	Subcategory	First Attempted CAS [1] N = 1092			First Attempted CEA [1] N = 1175		
		Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE	Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE
Stroke[2]		32	0	32	28	0	28
	Cerebral Hemorrhage, Ipsilateral	0	0	0	1	0	1
	Cerebral Hemorrhage, Non-Ipsilateral	2	0	2	2	0	2
	Ischemic, Ipsilateral	14	0	14	15	0	15
	Ischemic, Non-Ipsilateral	16	0	16	11	0	11
Trauma		11	14	25	11	8	19
Unadjudicated Stroke[2]		5	0	5	4	0	4
Unknown AE		6	1	7	6	0	6
Vascular		74	21	92	62	11	72
	Aneurysm	4	1	5	2	1	3
	Aortic Dissection	1	0	1	1	0	1
	Carotid Artery Disease	2	0	2	0	1	1
	Cerebral Malformation	0	0	0	0	1	1
	Contralateral Stenosis	31	6	36	27	1	28
	Deep Vein Thrombosis	1	1	2	2	0	2
	Peripheral Vascular Disease	21	9	28	18	7	24
	Renal Vascular Disease	1	0	1	6	0	6
	Target Lesion Restenosis	14	4	18	9	2	11
	Target Lesion Thrombosis	1	0	1	0	0	0
	Thrombosis	1	0	1	1	0	1

[2] The MI or stroke in the table are not primary endpoint events based on the definition of one year primary endpoint.

Table 15 (continued)

Category	Subcategory	First Attempted CAS ' N = 1092			First Attempted CEA ' N = 1175		
		Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE	Subjects with Serious AEs	Subjects with Non-serious AEs	Subjects with any AE
	Vessel Trauma	1	0	1	0	0	0

Table 16: Cause of Deaths Reported for All Enrolled Subjects

	Cause of Death	CAS	CEA
Death to 30 days			
	Stroke	4	4
	Bleeding	1	0
	Cardiac	2	0
	Sepsis	1	0
Death > 30 days			
	Stroke	3	5
	Bleeding	1	2
	Cancer	22	28
	Cardiac	34	22
	Drug overdose	1	0
	Gastroinstestinal	4	2
	Infection/Pneumonia	5	5
	Neurologic other than Stroke	3	2
	Renal Failure	5	5
	Respiratory Failure	12	9
	Sepsis	5	6
	Suicide	1	0
	Unknown AE outcome death	7	11
	Vascular	1	0
Total number of deaths		**112**	**101**

2. Effectiveness Results

The analysis of effectiveness was based on the CREST randomized population treated with CAS or CEA, with follow-up data available for 96.0% (2365/2464) of subjects at 1 month, 90.3% (2140/2369) of subjects at 1 year post-procedure, and 72.4% (589/813) of subjects at 4 years post-procedure.

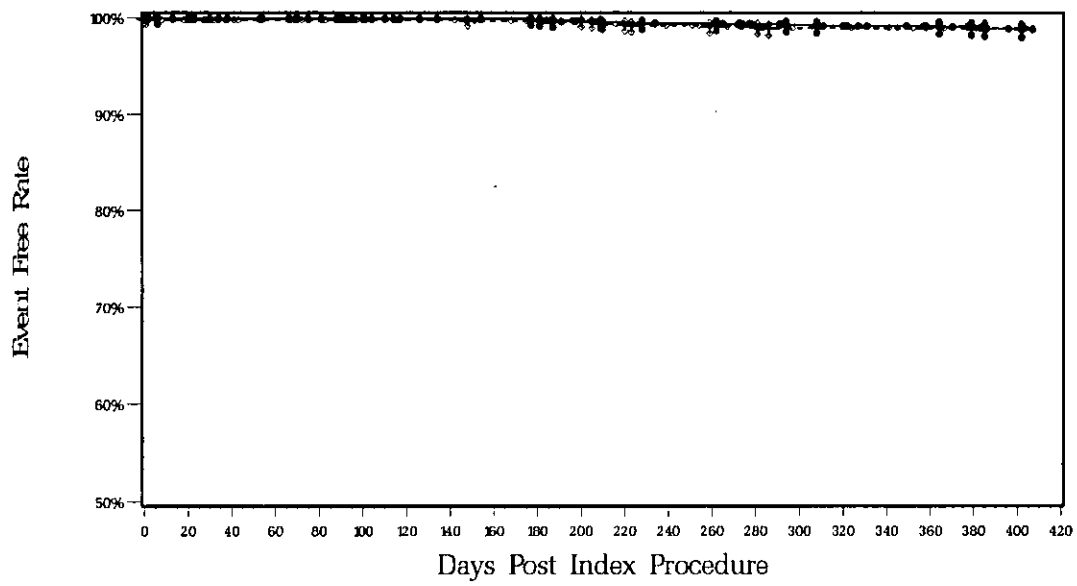
Effectiveness was analyzed by evaluating one-year clinically-driven target lesion revascularization (TLR) and 4-year long-term outcomes of a composite measure of all death, stroke, and MI at 30 days plus ipsilateral stroke between 31 days and 4 years.

Target Lesion Revascularization at 12 Months (PP population)

The freedom from clinically-driven TLR at 12 months by Kaplan-Meier Survival Analysis is 98.8% in the CAS arm and 99.0% in the CEA arm.

The Kaplan-Meier survival curves for the clinically-driven TLR in the CAS arm and the CEA arm at 12 months are comparable. The results demonstrate the long term durability of the CAS procedure compared to the conventional treatment with CEA in the standard surgical risk population requiring treatment for carotid stenosis.

Figure 7: CREST Freedom from Clinically-Driven Target Lesion Revascularization (TLR) at 12 Months (PP Population)



Solid line: CAS Subjects (n= 1131)
Dashed line: CEA Subjects (n= 1176)
Vertical bar: 95% Confidence Limit

Days Post Index Procedure	0	(0, 30]	(30, 180]	(180, 365]	(365, 407]
CAS					
Subjects at Risk	1131	1131	1119	1093	1060
Subjects Censored	0	11	25	25	1057
Number of Events	0	1	1	8	3
% Event Free	100%	99.9%	99.8%	99.1%	98.8%
% Standard Error	0.0%	0.1%	0.1%	0.3%	0.3%
CEA					
Subjects at Risk	1176	1175	1164	1141	1110
Subjects Censored	0	10	22	22	1110
Number of Events	1	1	1	9	0
% Event Free	99.9%	99.8%	99.7%	99.0%	99.0%
% Standard Error	0.1%	0.1%	0.1%	0.3%	0.3%
Tests Between Groups	Test	Chi-Square	DF	p-value	
	Log-Rank	0.096	1	0.7568	
	Wilcoxon	0.080	1	0.7778	

Note: Subjects at risk gives the number of subjects at risk of an event at the start of the interval, while subjects censored and number of events are the incremental counts of subjects censored or with events during the interval. The intervals are denoted as half-open bracket expression, where the start of interval '(' is exclusive and the end of the interval ']' is inclusive.

Long-term Outcomes of a Composite Measure of all Death, Stroke and MI at 30 days plus Ipsilateral Stroke between 31 Days and 4 Years

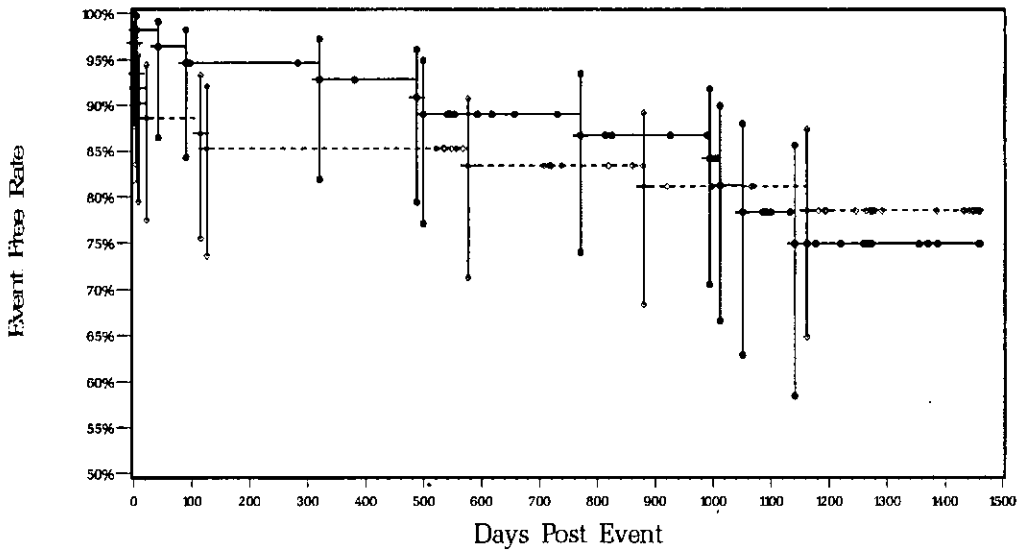
The long-term durability and effectiveness of the CAS treatment is consistent with that of conventional carotid endarterectomy. The 4-year long-term (median follow-up 3 years, with more than 500 subjects out to 4 years) composite endpoint event rates, DSMI plus ipsilateral stroke between 31 days and 4 years, are 8.8% in the CAS arm and 8.2% in the CEA arm for the PP analysis population with a HR 1.08. A similar result is also shown for the ITT analysis population in Table 17.

Table 17: Cox Proportional Hazards Analysis of Long-Term Outcomes

Analyses	Long-term Outcome (DSMI within 30 Days and Ipsilateral Stroke from Day 31 up to Four Years)		
	CAS Event Rate (%) ± SE (%) (N)	CEA Event Rate (%) ± SE (%) (N)	Hazard Ratio [95% CI]
Per-protocol	8.8% ± 0.91% (N = 1131)	8.2% ± 0.85% (N = 1176)	1.08 [-, 1.37]
Intent-to-treat	8.6% ± 0.85% (N = 1259)	8.5% ± 0.84% (N = 1237)	1.01 [-, 1.28]

Within the PP population, of subjects (N = 56) who experienced an MI within 30-days of their study procedure, there were 11 subjects who expired within 4 years, yielding an estimated freedom from death of 75.0% within 4 years, while the estimated freedom from death was 78.5% in those subjects who experienced a 30-day stroke (N = 62) . The difference of estimated freedom from death between the two groups is not statistically significant.

Figure 8: CREST Comparison of Freedom from Death within Four Years between Subjects with a 30-Day MI versus 30-Day All Stroke (PP Population)



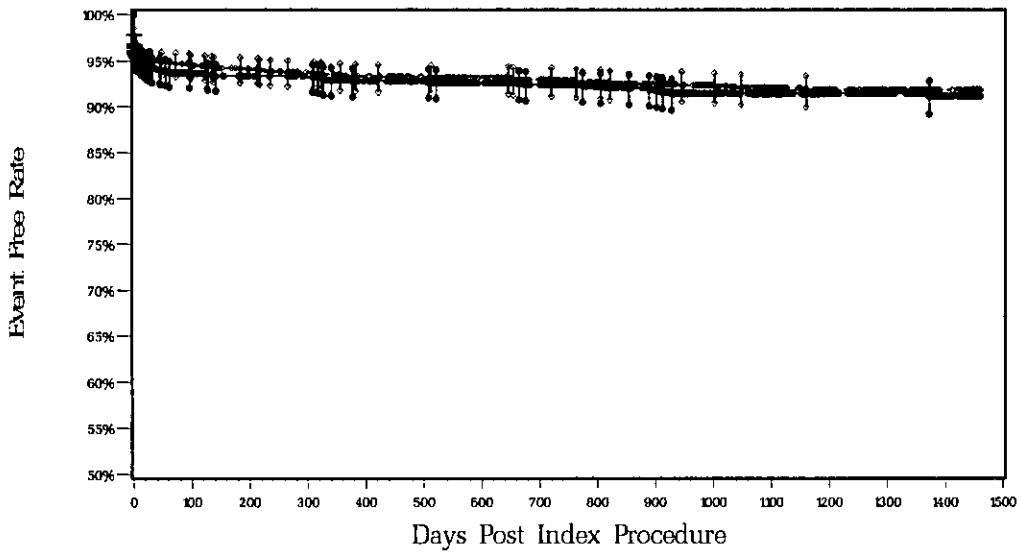
Solid line: MI Subjects (n= 56)
Dashed line: All Stroke Subjects (n= 62)
Vertical bar: 95% Confidence Limit

Days Post Event	0	(0, 365]	(365, 730]	(730, 1095]	(1095, 1461]
MI					
Subjects at Risk	56	56	50	40	25
Subjects Censored	0	2	8	11	24
Number of Events	0	4	2	4	1
% Event Free	100%	92.8%	89.0%	78.4%	75.0%
% Standard Error	0.0%	3.5%	4.2%	6.3%	6.9%
All Stroke					
Subjects at Risk	62	62	52	41	31
Subjects Censored	0	1	10	9	30
Number of Events	0	9	1	1	1
% Event Free	100%	85.3%	83.4%	81.1%	78.5%
% Standard Error	0.0%	4.5%	4.8%	5.2%	5.6%
Tests Between Groups	Test	Chi-Square	DF	p-value	
	Log-Rank	0.001	1	0.9703	
	Wilcoxon	0.188	1	0.6648	

At four years, the estimated freedom from endpoint events (DSMI within 30 days plus ipsilateral stroke between 31 days and 4 years) was 91.2% for the CAS subjects and 91.8% for the CEA subjects. The long-term durability and effectiveness of CAS has been confirmed to be consistent with conventional

carotid endarterectomy in the population of standard surgical risk subjects with disease in the internal carotid artery.

Figure 9: Freedom from Death, Stroke and MI within 30 Days and Ipsilateral Stroke from 31 Days up to Four Years (PP Population)



Solid line: CAS Subjects (n= 1131)
Dashed line: CEA Subjects (n= 1176)
Vertical bar: 95% Confidence Limit

Days Post Index Procedure	0	(0, 365]	(365, 730]	(730, 1095]	(1095, 1461]
CAS					
Subjects at Risk	1131	1094	1004	810	521
Subjects Censored	0	47	189	282	520
Number of Events	37	43	5	7	1
% Event Free	96.7%	92.9%	92.4%	91.5%	91.2%
% Standard Error	0.5%	0.8%	0.8%	0.9%	0.9%
CEA					
Subjects at Risk	1176	1150	1055	825	521
Subjects Censored	0	44	224	298	520
Number of Events	26	51	6	6	1
% Event Free	97.8%	93.4%	92.8%	92.0%	91.8%
% Standard Error	0.4%	0.7%	0.8%	0.8%	0.8%
Tests Between Groups	Test	Chi-Square	DF	p-value	
	Log-Rank	0.249	1	0.6176	
	Wilcoxon	0.286	1	0.5928	

3. Subgroup Analyses

The following preoperative characteristics were evaluated for potential association with outcomes: age, gender, and race.

Age

A multivariable analysis showed that age was a predictor for DSMI in both the CAS and CEA arms. This finding is comparable to results obtained from similar analyses of CAS data from high surgical risk populations. Age may be a surrogate for challenging vascular anatomy, such as a tortuous aorta and/or target carotid artery.

Age was also found to be a significant predictor of all four individual components of the primary CREST endpoint. In addition, symptomatic status and lesion length were predictors for stroke, and ischemic heart disease/congestive heart failure was a predictor for MI.

The results of the multivariable analysis show that age and diabetes were predictors for MI in the CEA arm. There were no predictors for the endpoint events of peri-procedural stroke, or death and major stroke identified for CEA.

Gender

An analysis of the composite endpoint in randomized subjects in the PP analysis population was performed to assess the interaction between revascularization treatment and gender. There were 64.6% (731/1131) male subjects in the CAS arm and 66.7% (784/1176) male subjects in the CEA arm of the PP analysis population.

Tables 18 and 19 present a summary of the primary and key secondary endpoints, stratified by gender. These analyses were not pre-specified. The results indicate similar event rates in the CAS and CEA arms across genders, as well as a similar treatment effect for males and females. No statistically significant interactions were found for the one year and the 30 day events by treatment and gender.

Table 18: Primary Endpoints by Gender and Treatment Arm (PP Population)

Analyses[1]	One Year Primary Endpoint Event Rate (%) ± SE (%) (N)		
	CAS	CEA	Difference [95% CI]
Per-protocol -- Male	6.74% ± 0.93% (N = 731)	6.14% ± 0.86% (N = 784)	0.60% [-1.88, 3.08%]
Per-protocol -- Female	7.78% ± 1.34% (N = 400)	7.49% ± 1.34% (N = 392)	0.29% [-3.43, 4.00%]

[1] Event rate is estimated by the Kaplan-Meier method and standard error is estimated by the Greenwood method.

43

Table 19: Death, Stroke and MI within 30 Days -- Events by Gender and Treatment Arm (PP Population)

Non-hierarchical Events	Male			Female		
	CAS N = 731	CEA N = 784	Difference [95% CI]	CAS N = 400	CEA N = 392	Difference [95% CI]
All Stroke	3.4% (25/729)	1.8% (14/783)	1.6%	5.3% (21/398)	2.0% (8/392)	3.2%
[95% Conf. Interval]	[2.2%, 5.0%]	[1.0%, 3.0%]	[0.0%, 3.3%]	[3.3%, 8.0%]	[0.9%, 4.0%]	[0.6%, 5.8%]
Minor Stroke	2.9% (21/729)	1.5% (12/783)	1.3%	3.8% (15/398)	1.5% (6/392)	2.2%
[95% Conf. Interval]	[1.8%, 4.4%]	[0.8%, 2.7%]	[-0.1%, 2.8%]	[2.1%, 6.1%]	[0.6%, 3.3%]	[0.0%, 4.5%]
MI	1.9% (14/729)	3.6% (28/783)	-1.7%	2.0% (8/398)	3.1% (12/392)	-1.1%
[95% Conf. Interval]	[1.1%, 3.2%]	[2.4%, 5.1%]	[-3.3%, -0.0%]	[0.9%, 3.9%]	[1.6%, 5.3%]	[-3.2%, 1.1%]
Death	0.5% (4/729)	0.1% (1/783)	0.4%	0.5% (2/398)	0.5% (2/392)	-0.0%
[95% Conf. Interval]	[0.1%, 1.4%]	[0.0%, 0.7%]	Assumptions not met	[0.1%, 1.8%]	[0.1%, 1.8%]	Assumptions not met

Table 20 presents the results of the Cox regression analysis of the interaction between treatment and gender for the one-year composite endpoint. There is no evidence of an interaction and the *p*-value for the interaction term was 0.9168. The result of the analysis indicates that there is no differential treatment effect modification between CAS and CEA in relation to the subject's gender.

Table 21 presents the results of a similar analysis of the interaction between treatment and gender for the secondary endpoint of 30-day DSMI.

Table 20: Interaction Analysis between Treatment and Gender on One-Year Composite Endpoint by Cox Regression (PP Population)

Variable	Coefficient (SE)	Hazard Ratio [95% CI]	*p*-Value[1]
Treatment (CAS vs. CEA)	0.06 (0.26)	1.06 [0.64, 1.76]	0.8233
Gender (male vs. female)	-0.19 (0.24)	0.83 [0.52, 1.31]	0.4182
Treatment * Gender	0.03 (0.33)	1.03 [0.54, 1.97]	0.9168

[1] Wald Chi-Square *p*-value.

Table 21: Interaction Analysis between Treatment and Gender on 30-Day DSMI by Cox Regression (PP Population)

Variable	Coefficient (SE)	Hazard Ratio [95% CI]	p-Value[1]
Treatment (CAS vs CEA)	0.38 (0.30)	1.46 [0.82, 2.61]	0.2028
Gender (male vs female)	0.08 (0.28)	1.08 [0.63, 1.86]	0.7787
Treatment * Gender	-0.41 (0.37)	0.66 [0.32, 1.38]	0.2711

[1] Wald Chi-Square *p*-value.

The analyses presented in Tables 18 – 21 suggest that it is valid to pool data for males and females, and that the overall results of this study can be generalized to both sexes.

Race

A retrospective analysis of the composite endpoint in randomized subjects in the PP analysis population was also performed to assess the interaction between revascularization treatment and race. The study enrolled a majority of Caucasians (N = 2159), with African-Americans being the next largest group (N=94). Since enrollment of subjects of other races was low, the analysis was done on African-Americans vs. Caucasians only.

Table 22 presents the results of the Cox regression analysis of the interaction between treatment and race for the one-year composite endpoint. There is no evidence of an interaction and the *p*-value for the interaction term was 0.2428. The result of the analysis indicates that there is no differential treatment effect modification between CAS and CEA in relation to the subject's race.

Table 22: Interaction Analysis between Treatment and Race on One-Year Composite Endpoint by Cox Regression (PP Population)

Variable	Coefficient (SE)	Hazard Ratio [95% CI]	*p*-Value[1]
Treatment (CAS vs. CEA)	0.11 (0.17)	1.11 [0.80, 1.55]	0.5206
Race (African-American vs. Caucasian)	0.69 (0.46)	2.00 [0.81, 4.96]	0.1342
Treatment * Race	-0.88 (0.75)	0.42 [0.10, 1.81]	0.2428

[1] Wald Chi-Square *p*-value.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

A. Panel Meeting Recommendation

At an advisory meeting held on January 26, 2011, the Circulatory System Devices Panel recommended that the Abbott Vascular PMA for the RX Acculink Carotid Stent System be approved. The Panel meeting transcript can be found at:

http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/CirculatorySystemDevicesPanel/ucm240575.htm.

The Panel recommended the following items be addressed in the labeling:

- The labeling should clearly state the number of patients evaluated at long-term follow-up visits.
- The labeling should emphasize the benefits of using an embolic protection device.

The Panel also provided the following recommendations for the post-approval study:

- The post-approval study should collect additional long-term data on patients and should be powered to assess results by symptomatic status.
- The post-approval study should evaluate the physician learning curve.

B. FDA's Post-Panel Action

FDA implemented all of the Panel's recommendations. The labeling includes a table summarizing the number of patients followed of those eligible at each follow-up time point. In addition, a statement has been added to emphasize that clinical study results

suggest lower event rates when the device is used in conjunction with an embolic protection device. A post-approval study design was developed which addresses the issues raised during the Panel deliberations. Specifically, the post-approval study will evaluate additional questions regarding the safety and effectiveness of the device based on patient symptomatic status, data will be collected on subjects through at least 3 years of follow-up to assess long-term outcomes, and an evaluation of the physician learning curve is incorporated in the study protocol.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Safety Conclusions

The adverse effects of the device are based on data collected in a clinical study conducted to support PMA approval as described above. The results from CREST demonstrate a reasonable assurance of safety for the RX Acculink System for use in standard surgical risk subjects with carotid artery disease. CREST met the primary endpoint of the trial in the primary analysis Per-Protocol population, as well as in all other analysis groups, e.g. the Per-Protocol Adjusted, Intent-To-Treat, As-Treated, and Modified As-Treated populations. FDA's review concluded that the adverse events observed and the rates of adverse events were acceptable and supportive of the primary objective results. This conclusion is consistent with the feedback provided to FDA by the Panel.

B. Effectiveness Conclusions

The results from CREST demonstrate a reasonable assurance of effectiveness for the the RX Acculink System for use in standard surgical risk subjects with carotid artery disease. Effectiveness of the device was analyzed by evaluating the one-year clinically-driven target lesion revascularization (TLR) and 4-year long-term outcomes of a composite measure of all death, stroke, and MI at 30 days plus ipsilateral stroke between 31 days and 4 years. The CREST study demonstrated that the rates of clinically-driven TLR at 12 months and long-term outcomes of the CAS treatment are consistent with that of conventional carotid endarterectomy.

C. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. CREST demonstrated that CAS is statistically non-inferior to CEA when performed using the RX Acculink Carotid Stent System with the Accunet Embolic Protection System to treat standard surgical risk subjects with disease in the internal carotid artery. Both long term and short term outcomes of CREST have established the safety and effectiveness of the RX Acculink Carotid Stent System for this supplemental pre-market approval application. FDA's Advisory Panel recommended that the benefit to the patient would outweigh the risk and that the PMA Supplement

be approved. FDA implemented all of the Panel recommendations for the labeling and post-approval studies.

XIII. CDRH DECISION

CDRH issued an approval order on May 6, 2011

A post-approval study involving use of the device according to its newly approved indication is required to obtain data related to the applicability of the clinical study data to the real-world patient population, detection of rare adverse events, and outcomes in clinically meaningful patient sub-populations. The results of this study will also be evaluated to determine whether any changes should be made to the device labeling to ensure that the information available to physicians is complete, appropriate, and up-to-date.

The final conditions of approval cited in the approval order are described below.

1. Abbott Vascular has agreed to conduct a non-randomized, multi-center study of the RX Acculink Carotid Stent System used in conjunction with Abbott Vascular's Accunet Embolic Protection System when used by a broad group of physicians in the population at standard risk for adverse events from carotid endarterectomy. Abbott Vascular has agreed to conduct the CANOPY trial, a post approval study that will include a minimum of 1,200 newly and sequentially enrolled subjects at up to 350 sites. The primary endpoint, which is the proportion of patients with a composite peri-procedural (within 30 days of the procedure) death and stroke, plus ipsilateral stroke between day 31 and 1 year (365 days), will be compared to a performance goal of 8.4%. Clinical follow-up for all subjects will be performed at 24-hours post-procedure, 30-days, 1-year, and annually for a total of 3 years. The secondary endpoints include the composite rate of death and stroke at 30 days post-procedure, ipsilateral stroke at 2 and 3 years post-procedure, and annual rates of clinically driven target lesion revascularization through 3 years post-procedure. Additional analyses include:
    a. a comparison of the peri-procedural death and stroke rates for symptomatic subjects and asymptomatic subjects to predefined performance goals for each group;
    b. a descriptive analysis of the peri-procedural death and stroke rate plus ipsilateral stroke at 1, 2, and 3 years for octogenarians; and
    c. a learning curve analysis based on information collected on operators' experience level.

2. Abbott Vascular has agreed to provide a clinical update to physician users at least annually until the last patient in their post-approval study has reached their final endpoint. Abbott Vascular will provide copies of these updates as part of their annual reports to FDA. At a minimum, this update will include a summary of the number of patients for whom data are available, with composite death and stroke rate at 30 days,

and ipsilateral stroke at 31 days to 365 days, and annually to 3 years, and rates for freedom from target lesion revascularization and device or procedure-related events.

The applicant's manufacturing facility was inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.